The science behind dry-cured ham quality: a literature review

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SUMMARY

Rapid urbanization, hectic lifestyles and the growth of processed food production account for the growing increase in unhealthy dietary habits worldwide. Diet is a modifiable risk factor of chronic disease and the principles that make up a healthy diet are universal. However, translating evidence into general nutritional advice for consumers can be a challenge for global health authorities. Nutrition requirements are highly individual and scientific studies frequently fail to isolate the effects of dietary factors of interest from broad food categories. For example, a considerable body of research has shown that processed meat is high in fat, salt and unhealthy additives that favor chronic disease development. Although such studies have provided sound data regarding the relationship between processed meat and human health, they have prevented food products made according to high quality processing standards from standing out. For example, several dry-cured hams have been awarded marks that certify their traditional quality and authenticity in terms of regional origin or traditional production (i.e. Protected Denomination of Origin or PDO). Among these, San Daniele ham, a PDO Italian product, has gained a large popularity at a national and international level.

The goal of this review is to discuss the science behind dry-cured ham. The review describes also the ongoing development of strategies for quality improvement and discusses the effects of consuming moderate portions of dry-cured ham as part of a balanced diet in a variety of health and disease settings.

Several variables of dry-cured ham production account for the quality of the final product. Pig genotype, feeding regime and diets, rearing system characteristics, slaughter procedures are the some of the most important ones. Genomic analysis helps identify the genetic mutations that affect the percentages of fat and lean mass. Consequently, by matching feeding regime and diet composition to genetic traits of pigs, meat producers can obtain thighs that are highly suitable for dry-cured ham production. Moreover, recent studies show that bedding, ventilation and pre- and post-slaughter treatments help prevent animal stress and its consequences on meat quality. Growing research shows also that proteolysis, lipolysis and lipid oxidation during curing impact texture, taste, aroma and properties of the final product.

According to Italian dietary guidelines, healthy individuals can consume up to 50 g of dry-cured ham up to twice a week, as part of a varied, balanced diet. Research has shown that dry-cured ham is rich in protein, iron and zinc, which can support tissue deposition for optimal growth and development. The mixture of protein, digestible amino acids, carnitine and creatine and many other compounds can also help adults and seniors maintain a healthy proportion of muscle mass. In addition, due to its content of protein, iron, magnesium, folate and antioxidant compounds, dry-cured ham could be a nutritious food during pregnancy. On the other hand, to eliminate any traces of pathogenic Listeria monocytogenes from the environment, pregnant women who choose to eat dry-cured ham should select products that have been cured for at least 12 months and heat slices up until steaming-hot. Furthermore, a growing body of research shows that dry-cured ham can help prevent some chronic diseases. For example, its high protein content may promote satiety, thus reducing the risk of diseases related to overeating. In addition, dry-cured ham contains bioactive peptides, which seem to have anti-hypertensive and antioxidant properties, and long-chain omega-3 fats, which may counteract inflammation, a major cause of chronic diseases.

In spite of the intrinsic limitations of studies in nutritional sciences, growing evidence from genomic and proteomic studies indicates that San Daniele ham and other PDO hams are relatively healthier foods within the processed meat category. Because of this, technicians and researchers should continue working towards dry-cured ham of higher quality and nutritional value. In the mean time, collaboration with nutrition professionals who translate evidence into practical nutrition advice may help consumers wisely incorporate dry-cured ham into a healthy lifestyle. The ultimate goal is to contribute to reduce the global burden of chronic diseases.
1. THE IMPORTANCE OF HAVING A HEALTHY LIFESTYLE

According to the Italian Ministry of Health and the World Health Organization (WHO), people who take good care of themselves are more likely to live healthier and longer. A healthy lifestyle includes a balanced diet, daily physical activity, non-smoking and moderate alcohol consumption. If everyone followed these principles, at least 80% of premature cardiovascular disease, 80% of type 2 diabetes and 40% of cancers could be prevented (WHO, 2009a; IMH, 2012). Nonetheless, unbalanced eating habits, physical inactivity, cigarette smoking and excessive alcohol consumption represent growing risk factors of chronic diseases worldwide (WHO, 2009b).

Global lifestyle trends are at least partially due to rapid urbanization, increased access to processed, high-fat, added-sugar, salt-laden foods and the increase in sedentary lifestyles. These modern risk factors of chronic diseases and are gradually replacing traditional ones like undernutrition or unsafe water (WHO, 2009b) (Figure 1a). Consequently, 65% of the world’s population live in a country where overweight and obesity is claimed to cause more deaths than underweight. More in detail, high blood pressure, high blood glucose, physical inactivity, overweight/obesity, high cholesterol and low intake of fruits and vegetables account for 19% of global deaths and 7% of global death-adjusted life years (DALYs) (Figure 1b). Of the six WHO regions, the European one is the most affected by chronic diseases, which, taken together, account for an estimated 86% of the deaths and 77% of the disease burden in the Region (WHO, 2006).

If the trends continue, by 2030 about 38% of the world’s adult population will be overweight and 20% will be obese. This is a cause of concern as excess body fat is a major risk factor for most chronic diseases (WHO, 2009a).

![Risk size](image)

Figure 1a: Transition of global health risks over time (Modified from WHO - Global Health Risks Report, 2009)
intake are highest in middle countries, as less than 5-2009b). Accordingly, a survey conducted in 2013 in the European region showed that none of the 33 countries ate less than 5 g of salt a day (EC, 2014). Similarly, the WHO reported that low fruit and vegetable intake are highest in middle-income European countries and in South-East Asia (WHO, 2009b). This is a

<table>
<thead>
<tr>
<th>Risk</th>
<th>World</th>
<th>Low and middle income countries</th>
<th>High income countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High blood pressure</td>
<td>12.8</td>
<td>12.1</td>
<td>16.8</td>
</tr>
<tr>
<td>High blood glucose</td>
<td>5.8</td>
<td>5.6</td>
<td>7.0</td>
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<td>Physical activity</td>
<td>5.5</td>
<td>5.1</td>
<td>7.7</td>
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<td>Overweight and obesity</td>
<td>4.8</td>
<td>4.2</td>
<td>8.4</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>4.5</td>
<td>4.3</td>
<td>5.8</td>
</tr>
<tr>
<td>Low fruit and vegetable intake</td>
<td>2.9</td>
<td>2.9</td>
<td>2.5</td>
</tr>
<tr>
<td>All 6 risks</td>
<td>19.1</td>
<td>18.1</td>
<td>25.2</td>
</tr>
</tbody>
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Percentage of DALYs

<table>
<thead>
<tr>
<th>Risk</th>
<th>World</th>
<th>Low and middle income countries</th>
<th>High income countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>High blood pressure</td>
<td>3.8</td>
<td>3.5</td>
<td>6.1</td>
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<tr>
<td>High blood glucose</td>
<td>2.7</td>
<td>2.5</td>
<td>4.9</td>
</tr>
<tr>
<td>Physical activity</td>
<td>2.1</td>
<td>1.9</td>
<td>4.1</td>
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<td>2.4</td>
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<td>1.1</td>
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<td>1.3</td>
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<tr>
<td>All 6 risks</td>
<td>7.0</td>
<td>6.5</td>
<td>12.6</td>
</tr>
</tbody>
</table>

Figure 1b: Global deaths and DALYs (Disability-Adjusted Life Years) attributable to 6 health risks. Data reported by region in 2004 (Modified from WHO - Global Health Risks Report, 2009)

1.1. Recommendations on diet and physical activity and related adherence

Although energy needs and nutrition recommendations depend on individual characteristics such as age, sex, cultural background and food availability, the principles that make up a healthy diet and an active lifestyle are universal. The Italian National Research Institute on Food and Nutrition (INRAN) and WHO agree that eating a plant-based diet rich in fresh produce, legumes, whole grains and dried fruit help prevent chronic disease development (INRAN, 2003; WHO, 2015a).

The Mediterranean diet originated in the countries that surround the Mediterranean sea and meets the healthy eating criteria set by global health authorities. According to the Mediterranean diet, more than half of total calories should derive from carbohydrates and, of them, at least 75% should be complex. While complex carbohydrates can be naturally found in vegetables, legumes, whole grains and dried fruit, simple carbohydrates or sugars are prevalent in industrial foods. Moreover, up to 30% of total energy intake should come from fats. In this regard, the intake of unsaturated fats, found in seafood, avocados, dried fruit and olive oil, should ideally account for no more than 30% of total diet energy (6-10% from poly-unsaturated fats or PUFA and 10-15% from mono-unsaturated fats or MUFA). Conversely, saturated fats (SFA), abundant in palm oil, coconut oil, meat, butter and dairy products, should account for no more than 10% of total energy intake. It is also recommended to avoid most trans fatty acids, which are common in industrial foods, and to limit cholesterol intake to 300 mg/day. Furthermore, it is recommended to consume no more than 5-6 g of salt (i.e. 2,300 mg of sodium) a day and drink about 1.5-2 l of water a day. Those who choose to drink alcohol should also remember that moderate alcohol intake means no more than 2-3 alcoholic units a day for men, no more than 1-2 alcoholic units a day for women and no more than 1 alcoholic unit/day for seniors (where 1 alcoholic unit corresponds to 12 g of ethanol or 125 ml of wine, 330 ml of beer and 40 ml of hard liquor). With regards to physical activity, it is recommended to practice at least 150 minutes of moderate physical activity a week or a combination of 75 minutes of vigorous aerobic activity and resistance training at least 2 days a week. In addition, children aged 5-17 should practice at least 60 minutes of moderate-to vigorous-intensity physical activity daily (WHO, 2010).

Unfortunately, a decline in the Mediterranean way of living has been reported (Dernini et al, 2015). This is consistent with the fact that unhealthy food choices alone are responsible of 50,000 deaths/year in Italy (IMH, 2012). More in detail, 51% of stroke and 45% of ischemic heart disease deaths are related to high systolic blood pressure, whose main risk factor is excess salt intake (WHO, 2009b). Average blood pressure levels are particularly high in middle-income European countries and African countries (WHO, 2009b). Accordingly, a survey conducted in 2013 in the European region showed that none of the 33 countries ate less than 5 g of salt a day (EC, 2014). Similarly, the WHO reported that low fruit and vegetable intake are highest in middle-income European countries and in South-East Asia (WHO, 2009b). This is a
cause of concern as insufficient intake of fruit and vegetables is thought to cause around 14% of gastrointestinal (GI) cancer deaths, about 11% of ischemic heart disease deaths and about 9% of stroke deaths globally (WHO, 2009b). Lastly, in 2013, 59% of the population reported to have never or seldom exercised or played a sport (EC, 2014). While physical activity can decrease the risk of cardiovascular disease, some cancers and type 2 diabetes; physical inactivity is most likely responsible of 21–25% of breast and colon cancer burden, 27% of diabetes and about 30% of ischemic heart disease burden (WHO, 2009b).

2. PROCESSED MEAT: A HETEROGENEOUS FOOD CATEGORY

Processed meat is a heterogeneous food category (Stettler et al, 2013). Therefore, it is important to differentiate among different processed meats.

2.1. Definition and health implications of processed meat

Red meat includes all mammalian muscle meat, such as beef, veal, pork, lamb, mutton, horse, and goat (WHO, 2015b). Meat is basically composed of water, protein, lipid, minerals and minimal amounts of carbohydrates. For example, water (72-76%) and protein (15-22%) are the major components of pork meat muscle and their proportion decreases as the amount of fat increases. In addition, pork lean muscle contains 1.5-4% fat (Toldrà et al, 2014). Processed meat, instead, refers to red meat or poultry that has undergone salting, curing, fermentation, smoking, or other processes to enhance flavour or increase preservation. Ham, hot dogs, ham, sausages, canned meat are all examples of processed meat (WHO, 2015b). Most biochemical changes occurring in meat curing depend on fresh muscle enzymes such as endopeptidases, exopeptidases, lipolytic enzymes, oxidative and antioxidant enzymes (Toldrà et al, 2014).

IARC (International Agency for Research on Cancer), an international advisory committee, has analyzed more than 800 scientific studies on cancer. According to IARC, red meat probably causes cancer while processed meat causes cancer (Figure 2). In fact, 34,000 deaths per year are attributable to processed meat intake and 50 g of processed meat a day can increase the risk of developing colorectal cancer by 18% (WHO, 2015b; IARC, 2018).

![Figure 2: Evidence regarding the relationship between meat and cancer (Modified from Cancer Research UK)](image)

Although IARC statements are based on sound evidence, the carcinogenic potential of N-nitroso compounds and polycyclic aromatic hydrocarbons derived from cooking and processing is still unclear. Few studies have thoroughly assessed whether or how different animals, animal parts or processing techniques can impact cancer development (WHO, 2015b). What is more, studies have shown that protective dietary compounds can mitigate meat’s impact on colon cancer, emphasizing the importance of designing studies that account for the composition of complex diets that include all consumed foods (Turner et al, 2017).
2.2. Recommendations on processed meat intake

The 2015-2020 Dietary Guidelines for Americans report that “eating patterns may include processed meats and processed poultry as long as the resulting eating pattern is within limits for sodium, calories from saturated fats and added sugars, and total calories” (ODPHP, 2015). Such statement is clear and sound; nonetheless, it does not address two important considerations.

First of all, the term “processed meat” includes food products derived from different animals and/or different cuts of the same animal. For example, according to numbers reported in the following table and resulting from the online food composition database of the United States Department of Agriculture (USDA, 2018), 100 g of sliced ham seem healthier than 100g of cooked bacon (with rendered fat) or salami (Figure 3).

<table>
<thead>
<tr>
<th>From the USDA Food Database</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ham</td>
</tr>
<tr>
<td>163 kcal, 16.6 g protein, 8.6 g fat, 1,143 mg sodium</td>
</tr>
</tbody>
</table>

Second, some processed meats are more popular in certain areas than others. Although IARC goal was to provide scientific evidence rather than nutrition recommendations, IARC statements about processed meat might have been differentially interpreted by the general public all over the world. For example, the 2014 Italian Recommended Intake of Energy and Nutrient (LARN), which represents the diet reference for the Italian population and healthy individuals, indicates that the standard serving size of traditional processed meats like dry-cured ham (prosciutto), mortadella and salame should be 50g, no more than 2-3 times a week (URSANU, 2015). More in detail, the guidelines clarify that 50g correspond to 3-4 medium slices of dry-cured ham, 5-6 medium slices of salame or 2 medium slices of mortadella (SINU, 2014). Altogether, it is unclear whether prosciutto, mortadella and salame are as carcinogenic as other processed meats that are more popular in other areas of the world.

3. DRY-CURED HAM: A UNIQUE KIND OF PROCESSED MEAT

According to the USDA, “ham is the cured leg of pork”. Of all kinds of ham, dry-cured ham is a special one as it involves the dry application of salt to fresh ham (USDA, 2012). The final product contains 18-23% fat, about 30% protein (depending on water and fat percentages) and at least 1,200 mg of sodium (Jiménez-Colmenero et al, 2010). Dry-cured ham is a typical food product in the Mediterranean area and is also relatively popular in the United States and Japan (Ivanovic et al, 2016). Although processing techniques vary from country to country and from region to region, dry-cured ham’s production is the result of two phases: the cold phase and the hot phase (Toldrà et al, 2007).

The cold phase involves the selection of raw material and the salting and post-salting steps. During salting, ham is refrigerated at 2-4°C (35.6-39.2°F) for 10–14 days to allow salt penetration. Marine salt helps remove water with the ultimate goal to reduce current volume and availability of “free” water to 0.95. The latter is called “water activity” or aw and normally ranges between 0 and 1. It also interacts with ambient humidity to prevent microbiological growth. During post-salting, the temperature is kept below 4°C (39.2°F) for 20-60 days to promote greater salt diffusion (Toldrà et al, 2007).

In the hot phase, instead, temperature rises to 14-20°C (57.2-68°F) and humidity reaches 70% to dry the product. Both of them activate biochemical reactions that promote ripening in the next 6-18 months. While Semimembranosus, an external muscle, dries up during the process due to water extrusion, Biceps femoris, an internal muscle, maintains a good level of residual moisture thus allowing enzyme activity (Toldrà et al, 2007).
3.1. PDO hams in the Mediterranean area

Italy, Spain and Portugal are the major producers of dry-cured ham in the Mediterranean area and then in the world. The most famous dry-cured hams from Italy are San Daniele and Parma hams. Instead, the most famous hams from Spain and Portugal include: Jamón Serrano (where jamón is the Spanish word for ham), Jamón de Guijuelo, Dehesa de Extremadura, Jamón de Huelva and Jamón Valle de los Pedroches from Spain and the Barrancos ham from Portugal (Toldrà et al., 2014).

Dry-cured hams from the Mediterranean area share common characteristics. First of all, Teruel Serrano ham (a particular type of Serrano) and all of the other hams mentioned above are endowed with the Protected Designation of Origin (PDO), a label that protects European Agro-food products of excellent quality and ensures that production phases and aging take place in a delimited geographic area (Toldrà et al., 2014, EU Parliament and Council, 2012). Second, they contain hundreds of mg of free amino acids per 100 g as a result of proteolytic reactions during curing (Jiménez-Colmenero et al., 2010). As further explained in paragraph 4.7, proteolysis byproducts not only contribute to the unique organoleptic profile of dry-cured ham but also play a functional role in the human body (Mora et al, 2016a). Third, dry-cured hams from the Mediterranean area significantly contribute to the consumption of healthy long-chain n-3 fatty acids (15.4-21.1% per 100g) (Jiménez-Colmenero et al, 2010). Lastly, they do not contain any additives or preservatives such as nitrates or peroxy-nitrates (Micha et al, 2012).

On the other hand, there are some differences among dry-cured hams from the Mediterranean area. While Parma, San Daniele and Serrano hams derive from intensively reared pig breeds, the other PDO hams (frequently referred to as “Iberian ham”) are obtained from extensively reared local breeds (Toldrà et al., 2014). Second, Iberian ham is characterized by a higher proportion of intramuscular fat (9.5%) compared to the hams obtained from the so-called white breed pigs, whose intramuscular fat content is lower than 4%. Furthermore, Iberian ham contains higher MUFA (54–58%, versus 35-40% in hams from white pigs), lower SFA (30–35%, versus 35-40% in hams from white breed pigs) and lower PUFA (8–12%, versus 10-15% in hams from white breed pigs) than Serrano and Italian hams (Jiménez-Colmenero et al, 2010).

4. DETERMINANTS OF PDO HAM QUALITY FOR HUMAN CONSUMPTION

Summarizing current literature regarding the quality determinants of PDO ham is key considering that health authorities have been sensitizing consumers to make healthier food choices. Indeed, the following paragraphs address all variables involved in pigs rearing and slaughter, green (i.e. uncured) ham production, curing and human consumption (Figure 4).
4.1. Pigs’ genotype

Pig thighs destined to make PDO ham must have excellent aptitude for salting and seasoning. Studying pig genotypes by selecting proper breeds and identifying the genes that determine fat composition can help improve the composition and flavour of the final product.

4.1.1. Breed

Pigs reared for dry-cured ham production have a higher percentage of body fat compared to those slaughtered for fresh meat consumption. Because of that, in Italy, it is possible to find “heavy pigs”, which are slaughtered at higher weights (150-160kg, 330-353 lb) to make dry-cured ham and other processed meats, and “light pigs”, which are slaughtered at 100-110 kg (220-243 lb) of body to obtain fresh meat (Stefanon et al, 2012).

Fat deposition in pigs occurs in multiple anatomical locations, as shown in the following Figure (Fontanesi et al, 2017) (Figure 5).

<table>
<thead>
<tr>
<th>Pig fat deposits</th>
<th>Subcutaneous or backfat (60-70%)</th>
<th>Inter-muscular (20-35%)</th>
<th>Peri-renal (5%)</th>
<th>Intra-muscular (&lt;5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrier to water diffusion and salt uptake</td>
<td>Determines consumers’ product acceptability</td>
<td>Plays a minor role on overall product quality</td>
<td>Responsible of marbling, plays a similar role to subcutaneous fat</td>
<td></td>
</tr>
</tbody>
</table>

Figure 5: Description, proportions and properties of fat deposits in pigs (Modified from Fontanesi et al, 2017)

Final quality of dry-cured ham results from subcutaneous and intermuscular fat proportions. Both fat types are composed of triglycerides, with small amounts of cholesterol (40–50 mg/100 g) (Toldrà et al, 2014). The subcutaneous fat depot (with a minimum of 15–20 mm depth) is also referred to as “backfat” and can be easily measured at the dorsal level. It helps moderate salt uptake and slow down moisture loss during processing thanks to a lower water diffusion rate (Fontanesi et al, 2017). Intermuscular fat, instead, is hard to trim from lean meat and can be measured only via post-mortem chemical analysis, image analysis...
or magnetic resonance (Fontanesi et al, 2017). On the other hand, intramuscular fat significantly affects final juiciness and consumer acceptability. Therefore, selecting breeds based on subcutaneous and/or intramuscular fat is important to achieve desirable carcass fatness. For example, Iberian ham is obtained from pure-bred and Duroc-crossbred Iberian pigs slaughtered at higher weights to obtain fatter carcasses (Toldra et al, 2014). Conversely, considering that excess fat in white breed pigs can negatively affect consumer acceptability, subcutaneous and intramuscular fat depots have been targeted as the main quality traits for dry-cured ham in the Italian Duroc heavy pig breeding program. Accordingly, pigs of industrial genotypes (Landrace, Large White, and other commercial crossbred pigs including Duroc as terminal sire) are slaughtered at lower weights to obtain leaner carcasses compared to their Iberian counterparts (Fontanesi et al, 2017). In particular, Landrace pigs have strong legs and are highly prolific, consistently with the intensive breeding procedures that characterize Italian dry-cured ham production (Stefanon et al, 2012).

Although intramuscular fat represents the least abundant fat depot in pigs, some studies have shown the potential of selecting breeds based on this fat depot. Intramuscular fat increases dry-cured ham’s juiciness and soft texture owing to tiny adipose cells that generate a marbling effect and act as a barrier to water diffusion and salt penetration (Ayuso et al, 2015; Candek Potokar et al, 2012; Hausman et al, 2014; Jiménez-Colmenero et al, 2010). Because Duroc pigs contain twice as much intramuscular fat than Landrace and Large White, it has been recommended to select pigs with about 50% Duroc genes and an ideal target of at least 2.5% intramuscular fat (Stefanon et al, 2012). However, marbling percentages in pigs selected for high lean deposition have decreased due to pork industry’s request to have a higher carcass lean cut amount and the fact that excessive intramuscular fat can cause excessive pastiness (Candek Potokar et al, 2012). Accordingly, the percentage of intramuscular fat in Longissimus muscle has lowered from 2-4% to 1% in Large White pigs since 1960s (Zappaterra et al, 2016). On the other hand, meat producers who wish to select Duroc breeds for higher levels of both lean mass and intramuscular fat should consider that the genetic correlation between these variables is between -0.25 and -0.37. In addition, intramuscular fat heritability is higher than or equal to 0.5 (Yang et al., 2011).

Different pig breeds can also lead to varied proteolytic activity during curing. Indeed, Iberian pig lines and Belgian Landrace pigs are characterized by lower activities of proteolytic enzymes compared to modern breeds and crosses (Candek Potokar et al, 2012). As explained in paragraph 4.7, low proteolysis can negatively affect meat quality. Conversely, cathepsin B (CTSB) protease and non-protein nitrogen are higher in Duroc pigs (Schivazappa et al, 2002). 

4.1.2. Individual gene effects

According to the Sscrofa11.1 assembly of the pig genome produced by the Swine Genome Sequencing Consortium (SGSC) in 2017, pig genome involves 22,452 coding genes, 3,250 non-coding genes and more than 64 million short variants (Ensembl, 2017). Although numerous genes account for carcass and meat quality, some distinctive genetic markers affect these parameters more than others. Indeed, single substitutions of DNA nucleotides (SNP) inside or outside gene-coding regions represent promising molecular markers to select the genetic traits that account for ideal proportions of fat and lean masses (Davoli et al, 2017).

The first most important SNP has been identified in a gene called RYR1. Such mutation causes an amino acid substitution in the ryanodine receptor responsible for the release of calcium from the sarcoplasmic reticulum, leading to intensive muscle contraction, thinner ham fat thickness, accelerated post-mortem glycolysis, decreased pH and lower water-holding-capacity (WHC). The latter is the water blocked in-between muscle filaments of different diameter. As further explained in paragraph 4.5, which describes slaughter procedures and post-mortem change from aerobic to anaerobic metabolism, RYR1 can lead to pale, soft, exudative (PSE) meat. A second well-known mutation affecting meat quality occurs in the PRKAG3 gene and is called RN- mutation. It causes an amino acid substitution in the AMP-dependent protein kinase which regulates glycogen content in muscle and is associated with leaner carcasses, lower muscle pH and reduced WHC (Candek-Potokar et al, 2012). These features can lead to dark, firm dry (DFD) meat (paragraph 4.5). Therefore, pig breeds like Pietrain, Belgian Landrace and Hampshire, which are frequently characterized by RYR1 and/or RN- mutation, are less suitable for dry-cured ham production due to higher leanness, thinner subcutaneous fat layer and higher seasoning losses (Candek-Potokar et al,
4.2.1 Veterinary inspections

An improvement of health status is expected in farms that apply strict isolation procedures. Pigs exposed to poor health conditions grow slower, consume less feed and have poorer feed conversion than healthy pigs. A study showed that poor health status decreased daily gain, feed intake, gain-to-feed ratio, lean deposition and feed intake by approximately 23, 10, 15, and 23%, respectively (Williams et al, 1997).

To improve pig health, veterinary inspections in the slaughterhouse ensure animal welfare, verify the audits carried out by the private sector and help discard legs from pigs affected by myopathy and other defects (Schnoeller et al, 2006). Veterinary inspections help also detect animal diseases such as viral agents of foot and mouth disease (FMD), classical swine fever (CSF) (hog cholera), African swine fever (ASF), swine vesicular disease (SVD), transmissible gastroenteritis of pigs (TGE) and porcine reproductive and respiratory syndrome (PPRS). Related risk assessments include the evaluation of agent susceptibility to pH and temperature, agent survival in specific pork organs and pork products, and the quantification of viral titers in relation to a minimum infective dose (Farez et al, 1997).
4.2.2. Immunity to PRRSV

PRRS, caused by the PRRS virus (PRRSV), has a major economic impact in dry-cured ham industry. PRRSV can cause reproductive failure in sows and respiratory illness in pigs of all ages and can be transmitted by oral consumption. The enveloped virus belongs to the Arteriviridae family within the Nidovirales order and is characterized by a single-stranded positive-sense RNA of approximately 15 kb. Although both the European genotype (Lelystad prototype) and the North American genotype (VR-2332 prototype) have been studied (Raymond et al, 2017), no effective vaccines have been developed so far. Two possible explanations are that infection with different strains can lead to diverse virologic and immunologic effects and that susceptibility of PRRSV strains to antibody neutralization is extremely variable (Piontkowski et al, 2016).

In order to characterize PRRSV infection in pigs, current research efforts are headed towards three directions. First, considering that both wild type and attenuated PRRSV induce a low level of cell-mediated immunity and that both vaccination or infection are followed by the secretion of low cytokine levels, research is currently focusing on IFN-γ and other cytokines in PRRS immunity (Diaz et al, 2006). Second, transcriptome studies, GWAS and meta-analyses have been implemented to study chromosome regions involved in the immune response to PRRS with the goal to genetically select pigs that are resistant to the virus. In this regard, preliminary results indicate that the first segment of the viral genome is strongly involved in host-virus interactions (Beura et al, 2010). Third, a large body of research is dedicated to the development of effective vaccines. Indeed, a recent study showed no significant differences in local or systemic reactions between young piglets (about 14 days of age) that had been administered a placebo or the novel type I PRRSV 94881-based MLV vaccine. In addition, compared with the placebo vaccinated piglets, vaccinated piglets challenged 14 days after vaccination with a virulent heterologous type I PRRSV isolate had significantly lower lung lesion scores, viremia, viral load in lung tissue, total clinical sign scores and a significantly greater average daily weight gain (Piontkowski et al, 2016).

4.3. Feeding regime and diet composition

Pigs’ feeding level (restriction), feeding pattern (restriction to re-feeding), diet composition and genetic potential can help determine their growth rate and the composition of weight gain (Lebret, 2008).

Feeding strategies of pigs involved in dry-cured ham production generally include three phases: growing-finishing (to promote lean mass deposition and achieve 80 kg/176 lb of live weight), fattening (until about the 30th week of age, to achieve about 130 kg/287 lb of live weight) and finishing (to promote intramuscular fat deposition until live weight reaches 160-180kg / 353-397 lb). Dietary requirements depend on tissue growth levels and are established according to the 2012 NRC (Nutrient Requirements of Swine) system, which focuses on ideal protein content, amino acid digestibility and net energy (NRC, 2012). This system has updated recommendations reported in the 1988 edition as well as the 1984 INRA (Institut National de la Recherche Agronomique) guidelines, which were based on raw protein and amino acid content and digestible energy (Stefanon et al, 2012).

Although pigs’ diet accounts for 60% of breeding costs (Fabro et al, 2014), no precise equations have ever been established to estimate the targets for protein deposition, protein-to-fat intake and total energy intake (Stefanon et al, 2012).

4.3.1. Feeding level and pattern

Fat deposition increases as pigs age while lean gain deposition increases as pigs advance in body weight up to approximately 60 kg (132 lb). After that, it decreases (Figure 6). As energy intake increases, protein deposition increases until a plateau. Then, fat deposition starts to prevail, especially when pigs reach 110-120 kg (243 – 265 lb) of body weight (Stefanon et al, 2012).
It has been proposed that restricted feeding (up to 35% compared to ad libitum feed intake) can reduce growth rate thus increasing age at slaughter at a given body weight. In fact, a 25% restriction in feed during the growing-finishing period decreases growth rate by about 27% (as protein deposition is almost constant in this phase). Instead, a restriction in feed allowance during the finishing period primarily affects fat tissue deposition, leading to a higher proportion of lean mass compared with ad libitum feeding. Instead, muscle fiber composition, glycolytic potential, pH and colour remain unaffected (Lebret, 2008). In the production of San Daniele ham, diet rationalization in the finishing period occurs via reduced feed intake or higher wheat bran-to-barley ratio in the feed. Both strategies are meant to prevent excessive fat deposition and preserve growth efficiency and muscle mass proportion in the carcass (Fabro et al, 2014, MIPAAF, 2007).

The level of animal response to a restriction to re-feeding pattern depends on its onset, duration and intensity as well as the onset and duration of re-feeding. If restriction occurs in the first 28-90 days, growth compensation and increased muscle protein turnover occur within the first 140 days of age. While restricted feeding affects more adipose tissue deposition than lean tissue deposition, compensation increases adipose tissue and internal organ growth without affecting lean mass. This is why re-fed pigs and control pigs can have similar carcass composition at slaughter. In addition, as the number of intramuscular adipocytes increases with age and intramuscular deposition increases with energy intake, increasing slaughter age and final energy intake via a “restriction and re-feeding” protocol is thought to enhance intramuscular fat level at slaughter. In this regard, many pig breeds destined to Iberian ham production are slaughtered at advanced age and finished during autumn in forests rich in starchy acorns and chestnuts (Lebret, 2008).

The importance of following an organized feeding plan based on pigs’ weight and growth rate was recently shown in an Italian project meant to enhance the traceability of local PDO ham in Friuli Venezia Giulia region, Italy. Based on the legislation to produce San Daniele ham, pigs born and reared in Friuli Venezia Giulia of up to 80 kg (176 lb) of live weight undergo a growing-finishing phase involving high quality protein and minerals in order to maximize growth. This is followed by a fattening phase including higher energy intake but lower protein and vegetable oil to promote muscle development and regular fat deposition until pigs body weight is as high as 130 kg (287 lb). At that point, pigs undergo a finishing phase and eat less protein (up to 12% of total energy intake) while total energy intake remains unvaried. In this phase, the level of efficiency of diet conversion is lower, leading to the right thickness of backfat and proper meat consistency by the ninth month of age (Stefanon et al, 2012) (Figure 7).
<table>
<thead>
<tr>
<th>Phase</th>
<th>Age (days)</th>
<th>Living weight (kg)</th>
<th>Growth (kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weaning piglet</td>
<td>30</td>
<td>11</td>
<td>0.35</td>
</tr>
<tr>
<td>Weaned piglet</td>
<td>80</td>
<td>32</td>
<td>0.43</td>
</tr>
<tr>
<td>Growing-finishing pig of lower weight</td>
<td>120</td>
<td>53</td>
<td>0.55</td>
</tr>
<tr>
<td>Growing-finishing pig of higher weight</td>
<td>190</td>
<td>100</td>
<td>0.69</td>
</tr>
<tr>
<td>Fattening pig</td>
<td>230</td>
<td>133</td>
<td>0.83</td>
</tr>
<tr>
<td>Finishing pig</td>
<td>270</td>
<td>170</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Figure 7: Living weight and ages of pigs reared to make San Daniele ham (Modified from Stefanon et al, 2012).

4.3.2. Diet composition

*Feed’s amino acid composition*

Amino acid composition is key to determine growth potential and lean mass development. As reported by Stefanon et al (2012), a 60 kg (132 lb) pig consuming a 300 g protein diet, can deposit 29.5% of ingested protein in muscle while almost 15% is excreted with stool and more than 50% in the urine (Stefanon et al, 2012). Lysine is the most limiting amino acid in swine diets so that the requirements for other amino acids are expressed as percentage relative to lysine (Figure 8A). Although amino acid requirements do not vary significantly with body weight (Figure 8B), diet supplementation with free lysine or methionine is frequently recommended to make sure the biological value of protein remains high (Stefanon et al, 2012).

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>Maintenance</th>
<th>Growth</th>
<th>Milk production</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lysine</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Histidine</td>
<td>32</td>
<td>32</td>
<td>40</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>75</td>
<td>54</td>
<td>55</td>
</tr>
<tr>
<td>Leucine</td>
<td>70</td>
<td>102</td>
<td>115</td>
</tr>
<tr>
<td>Methionine + cysteine</td>
<td>123</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>Phenylalanine + tyrosine</td>
<td>121</td>
<td>93</td>
<td>112</td>
</tr>
<tr>
<td>Threonine</td>
<td>151</td>
<td>60</td>
<td>58</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>26</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Valine</td>
<td>67</td>
<td>68</td>
<td>85</td>
</tr>
</tbody>
</table>

Figure 8a: Ideal amino acid intakes for maintenance, protein deposition and milk production in pigs (Modified from: NRC, 1998)
In the finishing phase, feeding pigs *ad libitum* with a lysine-deficient diet can improve tenderness and juiciness, increase intramuscular (and partially subcutaneous) fat, and reduce growth rate. Similarly, in the late fattening period, pigs given a lysine-deficient diet (5.6 versus 4g/kg lysine) about a month prior to slaughter have higher intramuscular fat levels and slightly higher backfat thickness than controls (Cisneros et al, 1996). Nonetheless, as noted by Lebret (2008), the study by Cisneros et al (1996) was conducted in pigs with high potential for intramuscular fat deposition (Lebret, 2008).

Compared to pigs fed *ad libitum*, a 25% caloric restriction in the growing-finishing period can lead to leaner carcases, lower intramuscular fat proportion and similar growth rate. Conversely, a combination of lysine deficiency and 20-25% caloric restriction increases pigs’ age at slaughter, thus promoting up to 40% intramuscular fat deposition without modifying backfat thickness or carcass lean meat content (Lebret, 2008).

Altogether, a progressive decrease in the lysine-to-energy ratio combined with reduced energy intake is recommended to improve carcase and muscle composition compared to an *ad libitum*, protein-deficient diet or, worst, reduced energy intake alone (Figure 9) (Lebret, 2008).

<table>
<thead>
<tr>
<th>Diet regime</th>
<th>Time</th>
<th>Pigs</th>
<th>Results (compared to <em>ad libitum</em> controls)</th>
</tr>
</thead>
</table>
| *Ad libitum* diet + lysine deficiency | 5 weeks prior to slaughter    | Pigs at high potential of intramuscular fat deposition | Lower growth rate  
                                        |                                | Much more intramuscular fat  
                                        |                                | Slightly more backfat          |
| 20-25% kcal restriction             | Growing-finishing             | Duroc crossbreds           | Unvaried growth rate  
                                        |                                | Less intramuscular fat  
                                        |                                | More lean mass                 |
| 20-25% kcal restriction + lysine deficiency | Growing-finishing             | Duroc crossbreds           | Higher age at slaughter  
                                        |                                | More intramuscular fat  
                                        |                                | Unvaried backfat               
                                        |                                | Unvaried lean mass             |

*Feed’s fat composition*

As pigs are mono-gastric animals, their diet can strongly affect the fatty acid composition of their adipose tissue (Candek Potokar et al, 2012). Hence, by feeding smaller proportions of SFA, larger proportions of MUFA or PUFA and a higher PUFA/SFA ratio, it is possible to improve the fatty acid profile and the sensory characteristics (appearance, texture and odour) of dry-cured ham (Jiménez-Colmenero et
al, 2010). For example, high supplementation of oleic acid (a MUFA) at 6% in concentrate feed let to softer fat. Moreover, enriching pork feed with long chain n-3 PUFA, such as linseed or marine oils, is thought to reduce the overall omega-6/omega-3 ratio of dry cured ham (Lebret, 2008). On the other hand, excess fat makes hams derived from White pig breeds like San Daniele, Parma and Serrano hams taste rancid. Indeed, a mixture of MUFA and conjugated linoleic acid (CLA, a naturally occurring trans fat in meat and meat products of ruminants) is thought to both limit rancidity and offset the increase in SFA caused by diets enriched with CLA alone (Lebret, 2008). On a side note, increasing evidence has showed that CLA consumption may have anti-carcinogenic and immunomodulatory effects in humans (Benjamin et al, 2009). Lastly, combining long-chain n-3 PUFA with vitamin E may help prevent ham rancidity due to cholesterol and/or lipid oxidation and minimize colour instability and altered WHC due to cellular membrane damages (Jiménez-Colmenero et al, 2010; Lebret, 2008).

Feed’s mineral composition

After energy and amino acids, phosphorus is one of the most important diet variables. Together with calcium, phosphorus plays an important role in bone mineralization. Its requirements can be estimated in two ways: by comparing endogenous losses to the phosphorus accumulated during growth or by assessing the responses obtained with variable phosphorus intakes. The calcium-to-total phosphorus ratio should be between 1-1.5 while the calcium-to-available phosphorus ratio should be 2.1-3.1. These parameters are important because high ratios limit phosphorus absorption (NRC, 1998). Moreover, although recommendations for calcium, total phosphorus and available phosphorus are largely based on NRC recommendations, about 25% of body phosphorus is in the muscles. Therefore, requirements depend on lean gain potential, with lean pigs requiring most phosphorus (NRC, 1998).

4.4. Rearing system

Besides being affected by diet, pigs are influenced by thermal, social, and management-related variables.

4.4.1. Thermal environment and ventilation

Air temperature, moisture and airflow are affected by space allowance, degree of building insulation and deep bed flooring.

The thermoneutral zone (TNZ) represents the range of temperatures within which a pig can maintain its normal body temperature of 39°C (102.2 °F) (Lebret, 2008) (Figure 10). Within the TNZ, pigs can control heat loss by regulating blood flow to the skin, huddling in groups and shifting posture. If temperature falls below TNZ, pigs shiver, eat more feed (if available) and grow less efficiently leading to more MUFA and less SFA in their backfat. Conversely, if temperature falls above TNZ, pigs reduce feed intake, increase water consumption and pant, thus reducing their backfat MUFA (Lammers, 2007). In addition, although cold temperatures are better tolerated than hot temperatures and help prevent bacterial growth, cold drafts from the outside can reduce overall humidity and reduce pigs’ growth rate (Lammers, 2007).

Last but not least, it has been shown that a 90 kg (200 lb) pig at an ambient temperature of 13°C (55°F) and in presence of deep bed flooring would experience the same thermal condition of another pig on a wet, solid, concrete floor at an ambient temperature of 26 °C (78°F).
4.4.2. Space allowance and other environmental characteristics

Small space allowance can lead to stressed pigs, dirty pens and suboptimal performance. Accordingly, the maximum number of pigs for a given area is generally reached when 1) at least one half of the lounge area is visible while all the pigs are standing, 2) one third of the floor space is visible when all the pigs are lying down and 3) there is one feeding space for every 4 to 6 pigs (Lammers, 2007).

Indoor environment affects growth performance and carcass traits too. Studies have shown that pigs reared on straw bedding (3.5 m²/pig) can stand lower ambient temperature and have easier access to the feeder compared to those reared to slatted floor (0.76 m²/pig), which leads to higher feed consumption, growth rate and carcass fatness (Lebret, 2008). In this regard, Maw et al (2001), studied the differences among bacon products obtained from different farms in Scotland, concluding that the bacon obtained from animals reared on straw bedding was greasier than that from pigs reared from slatted or concrete floor without bedding (Maw et al 2001). On the other hand, Patton et al (2008) showed that smaller increases of space allowance (up to 0.7 - 1.13 m²/pig) did significantly impact neither growth rate nor feed efficiency in a deep-beding finishing system (Patton et al, 2008).

Although indoor systems can guarantee better animal control, alternative housing systems with outdoor access have been investigated. The latter are thought to positively impact animal wellbeing as the outdoor environment promotes a more natural behaviour. Researchers have compared a sawdust-shave bedding system (1.3 m²/pig) characterized by free access to a sheltered outdoor area on concrete floor (1.1 m²/pig) with a conventional system characterized by slatted floor, 0.65m²/pig and controlled ambient temperature of 22.8°C (73°F). Compared to the conventional system, the new system improved growth rate due to higher feed intake, high backfat depth and lower lean meat content, which enhanced loin meat juiciness. However, there were no differences in pigs’ behavioral response to pre-slaughtering or slaughtering procedures (Meunier-Salau et al, 2006). Odour, flavour and tenderness remained unaffected too (Lebret, 2008).

In addition, studies mixing outdoor pigs with indoor pigs showed that mixing is less stressful for pigs that live outdoor. Accordingly, outdoor pigs seem less aggressive after mixing, leading to less skin lesions, higher pre- and post-mortem muscle glycogen and lower pH (Lebret, 2008).

As far as organic rearing is concerned, studies have shown that the eating quality of organic pork is extremely variable and mostly influenced by feeding management rather than housing conditions (Lebret, 2008).

4.5. Slaughter

Ante- and post-mortem stressors can lead to meat defects of two types: PSE (pale, soft, exudative) or DFD (dark, firm, dry). While reducing ante-mortem stressors can help raise meat quality, minimizing post-mortem factors can improve consumers’ perceived quality (Sionek et al, 2016).

4.5.1. Pre-slaughter
When animals experience ante-mortem stress, the sympathetic part of their autonomic nervous system stimulates the hypothalamus–pituitary gland–adrenal cortex leading to increased secretion of adrenaline and noradrenaline (Foury et al, 2011). The most stressful ante-mortem procedures include loading, transport, unloading and pigs surveillance at the lairage. Other pre-slaughter variables include weather, time of the year, pre-slaughter fasting and gender (Figure 11).

<table>
<thead>
<tr>
<th>Factor</th>
<th>Incidence of defective meat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term stress</td>
<td>↑ DFD</td>
</tr>
<tr>
<td>Short-term stress</td>
<td>↑ PSE</td>
</tr>
<tr>
<td>Low density loading factor (m²/100kg)</td>
<td>↑ PSE</td>
</tr>
<tr>
<td>Transport of pigs from different herds</td>
<td>↓ PSE, ↑ DFD</td>
</tr>
<tr>
<td>Prolonged stay at a lairage</td>
<td>↑ DFD</td>
</tr>
<tr>
<td>Summer</td>
<td>↑ PSE</td>
</tr>
<tr>
<td>Winter</td>
<td>↓ PSE, ↑ DFD</td>
</tr>
<tr>
<td>Ante-mortem fasting &gt; 14 hours</td>
<td>↑ DFD</td>
</tr>
<tr>
<td>Females/castrates</td>
<td>↑ DFD</td>
</tr>
<tr>
<td>Males</td>
<td>↑ PSE</td>
</tr>
</tbody>
</table>

Figure 11: Impact of pre-slaughter factors on meat defects (Modified from: Sionek et al, 2016)

When pigs are transported to the lairage, loading density should not exceed 0.425 m²/100 kg of pig weight to minimize acute stress and allow pigs to stand or lie in their natural positions (EU Council, 2005). According to Guardia et al (2005), reducing the loading factor from 0.5 to 0.37 m²/100 kg minimizes DFD defects by 11% (Guardia et al, 2010). On the other hand, a low density loading factor (m²/100kg) is inversely related to PSE defects, which are higher when transport lasts three hours or less. What is more, both DFD and PSE defects are more frequent when pigs are transported in cars endowed with metal rather than polyester floor due to higher noise level and slipping risk (Guardia et al, 2005).

Transporting pigs from different herds increases the risk for DFD but not PSE defects as animals tend to fight more during transport (Terlouw et al, 2005). While resting for about 2-3 hours prior to slaughter is recommended (Sionek et al, 2016), a resting time longer than 9 hours can cause DFD defects (Guardia et al, 2005).

Contrary to loading density and transport, the influence of weather and time of the year is more difficult to interpret. Guardia et al studied almost 16,000 pigs and noticed that the frequency of incidence of PSE defects is twice as higher in summer than in winter, possibly because pigs lack sweat glands (Guardia et al, 2004). On the other hand, other studies have shown that the incidence of PSE defects is higher in wintertime (33% versus 25.5%), possibly because the rate of slaughter is higher around Christmas time thus increasing animal stress (O’Neil et al, 2003).

Ante-mortem fasting and gender are the least explored variables. In some countries, animals are forced to fast for about 12-15 hours prior to transport in order to prevent bacterial spoilage and DFD defects (Sionek et al, 2016). On the other hand, fasting practices longer than 14 hours can make pigs more aggressive, thus causing DFD defects (Guardia et al, 2005). In addition, non-castrated males have higher energy reserves than females or castrated males, which explains why Guardia et al (2005) found that DFD incidence was 7% higher in females and castrated males than in non-castrated males (Guardia et al, 2005).

4.5.2 Slaughter and post-mortem procedures

Peri-mortem pH can strongly impact meat quality. While the recommended pH range for curing is
5.6-6.2 (Stefanon et al, 2012), pH variations can affect both WHC (indirectly) and enzymatic activities (directly) (Lebret, 2008). When post-mortem pH is between 5.6 and 6, WHC decreases leading to PSE meat and, consequently, higher processing losses and salt intake. Lower pH values can also promote lysosome breakage, enzymatic release and excessive muscle proteolysis, generating tyrosine crystals and a white film on vacuum-packed ham. Conversely, when post-mortem pH is higher than 6.2, meat becomes DFD, bringing about unpleasant softness due to bacterial spoilage, higher water activity and reduced enzymatic activity (Lebret, 2008).

Pig stunning is carried out in two ways: electrical or with the use of carbon dioxide gas. Electric stunning can cause PSE defects. What is more, the longer the application of electric current, the higher protein denaturation and drip loss (Van de Perre et al, 2010). In fact, Channon et al (2002) noticed an increase in PSE defects after a 19-second electric shock to the head compared to a 4-second electric shock or carbon dioxide stunning (Channon et al, 2002). Instead, the timing of carbon dioxide-based stunning has not been studied yet.

After pig stunning, bleeding should be carried out as soon as possible to prevent animals from regaining consciousness. Multiple studies have shown that hanging pig carcasses by the pelvis can help sarcomeres stretch to a greater extent than hanging them by their Achilles tendon (Channon et al, 2014). In addition, electrical stimulation prior to cooling may decrease pH faster which means that meat cooling should be very quick to prevent PSE defects (Sionek et al, 2016). For example, Springer et al compared the application of -32°C (-25.6°F) for 60, 90, 120 and 150 minutes and then 2°C (35.6°F) for another 24 hours. Quick cooling increased pH and WHC so that colour, texture and firmness improved (Springer et al, 2003). On the other hand, Sionek et al reported that, when cooling is too quick, tissue water distribution can be negatively affected (Sionek et al, 2016).

4.6. Curing ingredients
According to health authorities, consumers should eat foods that are as close as possible to the natural state of ingredients. Hence, additives are controversial ingredients in dry-cured ham production.

4.6.1. Salt and salt substitutes
Salt (i.e. sodium chloride, NaCl) acts as preservative, prevents the growth of Clostridium botulinum and Listeria monocytogenes, inhibits cathepsins and aminopeptidases and provides dry-cured ham with a unique flavour and texture. Salting procedures cause the extrusion of water, which allows salt to diffuse towards the inner part of muscle. Then, during curing, superficial water is released and inner water content starts to equilibrate (Candek-Potokar et al, 2012; Safa et al, 2017).

Although high levels of subcutaneous, inter- and intramuscular fat (IMF) can act as barrier to water diffusion and salt penetration (Candek-Potokar et al, 2012), meat producers have been studying how to reduce salt without affecting fat content. Four main strategies have been identified so far: 1) combining sodium chloride with other salts (potassium chloride, calcium chloride, magnesium chloride, potassium lactate or calcium ascorbate) 2) replacing salt with flavour enhancers, 3) decreasing salt crystals’ size by 10- to 100 fold to accelerate their dissolution in the mouth, and 4) prolonging the curing phase (Rama et al, 2013; Safa et al, 2017).

Although attempts to reduce sodium content were successful in the past (Figure 12), researchers have come up against several challenges in the attempt to further reduce salt percentage.

<table>
<thead>
<tr>
<th>Year</th>
<th>San Daniele ham</th>
<th>Other Italian dry-cured hams</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>2011</td>
<td>4.5</td>
<td>6</td>
</tr>
<tr>
<td>Salt reduction %</td>
<td>-36%</td>
<td>-15%</td>
</tr>
</tbody>
</table>

Figure 12: Salt content of Italian dry-cured ham in 1993 and 2011 (Assica, 2013)

First, substituting sodium chloride with 30% potassium chloride can make ham taste bitter (Gou et al, 1996). Second, yeast extracts or taste enhancers promote bacterial growth and negatively affect texture.
Nitrite and nitrate (a precursor of nitrite) impact appearance and quality of cured meats, providing them with the taste and odour characteristic of salted-dried products. Nitrite alone 1) provides a reddish-pink colour due to the binding of nitric oxide to myoglobin, 2) has a bacteriostatic action on Clostridium, Salmonella and coliforms, and 3) limits lipid oxidation, thus retarding cured meat rancidity. In spite of these positive effects, however, nitrite is toxic at large doses as it converts hemoglobin into methemoglobin, which prevents oxygen transport to body tissues. In addition, it combines with amines from meat proteolysis at 130 °C (266°F) and in acidic medium, thus forming carcinogenic nitrosamines (Safa et al, 2017).

Considering that nitrate and nitrite are lethal at doses of 80-800 mg/kg body weight and 33-250 mg/kg body weight respectively (Safa et al, 2017), the WHO has established that acceptable daily intake (ADI) levels of nitrate and nitrite are 3.7 mg/kg body weight/day and 0.07 mg/kg/day, respectively. Such recommendations are based on drinking water standards. In fact, water and vegetables are the major sources of dietary nitrate (70-90%). While spinach contains 740 mg nitrate/100g (7400 ppm), there are only 156 ppm, 120 ppm and 0.5 mg of nitrite in sausages, bacon and hot dogs, respectively. In addition, our saliva helps generate additional nitrite from nitrate reduction (Bedale et al, 2016).

Considering that the health effects from nitrite/nitrate have not been fully elucidated yet, researchers have been studying the pros and cons of removing such additives from dry-cured ham. Unfortunately, available data indicate that their removal is far from a trivial issue as it could cause colour alterations and survival of Gram-negative bacteria (Pichner et al, 2006). Similarly, substituting nitrite/nitrate with nitrate-rich powdered vegetables (celery, beetroot, and leek, among others) can impair meat palatability and consistency (Toldrà et al, 2014).

Conversely, Parma and San Daniele hams are nitrite/nitrate-free, bright red and microbiologically safe, especially when refrigerated (Bedale et al, 2016). As Wakamatsu et al (2010) noted, these hams owe their colour to zinc protoporphyrin IX (ZPP; 60-70% of all porphyrins), a molecule that resembles heme with the difference that iron has been replaced by zinc, a metal abundant in pork. Interestingly, nitrite added to dried-cured pork products can lead to the formation of nitric oxide (NO), an inhibitor of protoporphyrin IX (Wakamatsu et al, 2010).

4.7. Biochemical reactions during curing
Most dry-cured ham characteristics result from proteolysis and lipolysis that occur during curing, as explained in the following paragraphs.

4.7.1. Proteolysis and resulting bioactive peptides
It has been published that dry-cured ham contains short sequences of at least 2-20 amino acids that are released from muscle proteolysis during meat curing processes (Martínez-Sánchez et al, 2016).
Proteolysis starts with an initial breakdown of major myofibrillar proteins by endopeptidases like lysosomal proteinases (e.g. cathepsin B, D, H, L), neutral proteinases (e.g. calpains) and proteasome. Resulting peptides are digested by exopeptidases like tripeptidylpeptidases, dipeptidylpeptidases, dipeptidases, carboxypeptidases and aminopeptidases (Mora et al 2016a; Toldrà et al, 2006). The level of proteolysis in dry-cured ham is summarized by a numerical value called “proteolysis index” (100×non-protein nitrogen/total nitrogen). The latter decreases at high sodium chloride concentrations, thus explaining the relationship between water content and texture parameters such as hardness, cohesiveness and springiness (Ruiz Ramirez et al, 2006).

**Peptides with anti-hypertensive properties: in vitro evidence**

Growing research indicates that many peptides generated from proteolysis can be referred to as bioactive as they can exert important biological effects in vitro and in vivo. For example, bioactive peptides can inhibit angiotensin I-converting enzyme (ACE), which transforms angiotensin I into angiotensin, a vasoconstrictor, and promote the degradation of bradykinin, a vasodilator (Scalese et al, 2016) (Figure 13).

![Figure 13: Mechanism of action of ACE-inhibitors (Modified from Scalese et al, 2016)](image)

An in vitro study compared aqueous peptide extracts from Teruel, Parma and Belgian hams. Such extracts were fractionated by size-exclusion chromatography so that a fluorimetric assay could estimate the hydrolysis of an internally quenched fluorescent substrate by the action of ACE. Researchers found that the ACE inhibitory activities of peptide fractions were 93%, 70 and 76% respectively, which indicated their anti-hypertensive potential (Mora et al, 2016b). Another study involving simulated GI digestion of Parma ham identified 81 different peptide sequences (21 dipeptides and 12 triptides) derived from myofibrillar and sarcoplasmic proteins with a molecular weight of 200-1,700 Da. According to migration experiments in Caco-2 cells, 55 of these peptides were able to translocate from the apical to the basolateral compartment of the intestinal epithelium after 60-120 minutes. These data indicate that bioactive peptides may exert systemic anti-hypertensive effects as they cross the intestinal epithelium. What is more, by using a combined in vitro-in silico approach, the same researchers were able to predict bioactive peptides’ sequences, finding that Lysine-Glycine-Lysine (LGL) was the most active peptide and that its IC₅₀ (i.e. the dose at which 50% of ACE activity is inhibited) was 145 microM. Based on that, the researchers estimated that there are 62 mg LGL/g in 24 month-cured ham and 112 mg LGL/g in 18-month-cured ham respectively. In other words, a slice of ham (15g) contains 930-1,680 mg of LGL peptide (62-112mg x 15g) with anti-hypertensive potential (Paolella et al, 2015).

**Peptides with antioxidant properties: in vitro evidence**

In vitro studies suggest that bioactive peptides have metal-chelating or hydrogen/electron donating properties. In other words, they may help prevent and/or block radical chain reactions as part of enzymatic defense systems against reactive oxygen species (Figure 14).
Paolella et al (2015) evaluated the ability of digested Parma ham samples to act as radical scavengers by using the ABTS assay. The latter measures the ability of antioxidants to scavenge the ABTS generated in aqueous phase, as compared with a water-soluble vitamin E analogue. The ABTS is generated after that a strong oxidizing agent reacts with the ABTS salt so that the reduction of blue-green ABTS radical colored solution is measured by the inhibition of its characteristic long wave (734 nm) absorption spectrum (Shalaby et al, 2013). Thanks to this assay, the researchers noticed a strong increase in antioxidant activity in the basolateral compartment of Caco-2 cells after 30 minutes and such activity increased from 60 to 120 minutes (Paolella et al, 2015). Similarly, Escudero et al (2013) pooled peptides extracted from Spanish dry-cured ham and utilized reversed-phase chromatography and nano-LC-MS/MS analysis (i.e. Liquid Chromatography, Mass Spectrometry) to study the sequence of the peptides with the highest 1,1-diphenyl-2-picrylhydrazyl (DPPH) scavenging activity. DPPH is a stable free radical with maximum absorbance at 517 nm. As soon as it interacts with an antioxidant, absorbance decreases and radical-scavenging potential is revealed (Escudero et al, 2013). Thanks to the DPPH assay, the researchers identified 27 peptides and the strongest radical-scavenging activity was observed with the peptide SAGPNP (Ser-Ala-Gly-Asn-Pro-Asn) which exerted 50% antioxidant activity at a concentration of 1.5mg/ml. Instead, the peptide GLAGA (Gly-Leu-Ala-Gly-Ala) had higher reducing power with 0.5 units of absorbance at 700 nm at a concentration of 1mg/ml (Escudero et al, 2013). Interestingly, other authors noticed that hydrophobic amino acids and one or more residues of His, Pro, Cys, Tyr, Trp, Phe or Met might enhance overall antioxidant potential (Ren et al, 2008) as they are compatible with the active sites of ACE contrary to hydrophilic amino acids (Paolella et al, 2015).

Many studies on ham anti-oxidant peptides have been conducted on Chinese hams too. A study on Xuanwei ham, utilized size exclusion chromatography, anion exchange column and reversed-phase High Performance Liquid Chromatography (HPLC) to separate fractions by molecular weight and polarity differences. The researchers utilized also LC-MS/MS to assess any scavenging effects on hydroxyl (OH) radicals, superoxide anion O2(-), and DPPH. The researchers concluded that Xuanwei ham has a strong antioxidant activity during curing and that the peptide ALGG (Asp-Leu-Glu-Glu) plays a key role in the scavenging process (Xing et al, 2015). Similarly, a study of Jinhua ham extracts showed that GKFNV (Gly-Lys-Leu-Asn-Val) had 92.7% antioxidant activity at a concentration of 1 mg/ml. In addition, LPGGHGDGL (Leu-Pro-Gly-Gly-His-Gly-Asp-Leu) had the highest hydroxyl radical scavenging activity, LPGGTT (Leu-Pro-Gly-Gly-Gly-Thr) and HA (His-Ala) inhibited 45% of erythrocyte hemolysis before digestion and KEER (Lys-Glu-Glu-Arg) contributed to Fe^2+ chelating ability after GI digestion (Zhi et al, 2015).

*In vivo evidence on antihypertensive and/or antioxidant peptides*

Escudero et al (2012) assessed antioxidant effects and changes in systolic blood pressure of spontaneously hypertensive rats after oral administration of a fractioned peptide extract obtained from Spanish dry-cured ham. All samples exhibited anti-hypertensive activity and pooled fractions of 1,700 Da or
lower were the most anti-hypertensive and associated with a 38.38 mmHg drop in systolic blood pressure. In addition, some fractions exhibited 39-92% DPPH radical-scavenging activity and 41.67-50.27% superoxide ion extinguishing ability. The antioxidant activity of peptides of 500–1500 Da was stronger than that shown for peptides of more than 1500 Da or less than 500 Da. In other words, peptides with a weight of 500-1700 Da are more likely to cross the intestinal barrier (Escudero et al., 2012). Thus, in vivo evidence supports in vitro studies suggesting that dry-cured ham is a source of bioactive peptides that may help counteract oxidative stress and the adverse effects of sodium chloride on human blood pressure. On the other hand, human studies are needed to confirm these results.

4.7.2. Lipolysis and lipid oxidation

The intensity of lipolysis and oxidation during dry-cured ham processing varies based on the length of salting procedures and the characteristics of the ripening environment.

Lipolysis affects lipid structure in several ways. Phospholipids, the main substrates for lipolysis, are hydrolysed by phospholipases and lyso-phospholipases. Triglycerides and diglycerides, instead, are hydrolysed by lipoprotein lipase (in the blood vessels), hormone-sensitive lipase (in the cytosol) and acid lipase (in the lysosomes). While very little is known about how phospholipases work in skeletal muscles post-mortem, it is well-known that hormone-sensitive lipase and acid lipase are more active in oxidative than in glycolytic muscles. The lipolytic process ends with a monoacylglycerol lipase which hydrolyzes resulting monoglycerides. Such process is faster during the first 6 months of curing so that fatty acid concentration rises from 1% to up to 12% of total lipids in adipose tissue and from 1% to 8-20% of total lipids in muscle tissue. While neither diet nor live weight affect lipolysis, longer processing stages and high temperatures can increase the concentration of fatty acids (Gilles et al., 2009).

Contrary to lipolysis, lipid oxidation involves mostly PUFA (Gilles et al., 2009) and can generate both pleasant volatile compounds (especially in the first months of curing) and undesired effects such as protein aggregation, myoglobin oxidation and free radical formation (Ventanas et al., 2005) (Figure 15). While aldehydes are responsible of rancid, fruity, and green aroma, methyl-ketones provide pleasant aged and dry-cured ham odour. In addition, while vitamin E inhibits lipid oxidation; high temperatures, long drying and ripening, high salt concentration and low muscle pH promote lipid oxidation. Accordingly, hams with a short curing period (9-12 months), such as Parma ham, may have a fresh fat aroma while hams with a curing process of more than 18 months, such as Corsican and Iberian hams may have stronger “rancid”, “cured” and “mushroom” aroma notes (Gilles et al., 2009).

To assess the impact of lipid oxidation, an Italian study compared the sensory features and volatile composition of San Daniele, Parma and Toscano hams. San Daniele and Parma hams had higher scores of sweetness, RGB (red-green-blue) colour values and water activity compared to Toscano ham. While Parma ham stood out for its cured flavour, Toscano ham had higher scores of pork-meat odour, saltiness, dryness, fibrousness and hardness, possibly due to the higher levels of salt content, instrumental hardness, cohesiveness and chewiness (Laureati et al., 2014). San Daniele ham, instead, showed a larger fatty area and a higher pH value compared to the other kinds of ham. Another study involving headspace GC–MS (Gas
Chromatography-Mass Spectrometry) technique showed that San Daniele ham has eight unique volatile compounds: 4-methyl-1-penten-3-ol; 2-methyl-2-pentenal; 2-ethylhexanone; allyl acetate; propylformate; amyl formate; isobutyl acetate; methylthiomethane. Such compounds as well as the highest percentage of alcohols are relatively uncommon in Mediterranean dry-cured hams. Instead, branched and linear aldehydes (i.e. hexanal and pentanal) were the second most abundant group of volatile compounds (31.53%), thus confirming data reported for other European hams. In addition to that, almost 10% of the volatile fraction consisted of ketones and acetone, i.e. the ketone responsible for the buttery flavour of cooked meat, was the most concentrated. Lastly, San Daniele ham had low levels of esters, possibly owing to salting and curing procedures, as well as therpenes and nitrogen compounds, probably due to animal feed and analytical limitations (Gaspardo et al, 2008).

4.8. Other characteristics of the final product

Ham’s visual appearance and microbiological profile are key to determine consumer acceptance and safety.

4.8.1. Weight and visual appearance

Although heavier hams have lower seasoning losses, a recent study on 10.1-11.9 kg (22-26 lb) hams coming from Slovenian commercial fatteners, showed that weight alone did not have any significant influence on processing losses during separate processing phases (Candek-Potokar et al, 2011). In addition, comparisons between pressed and unpressed Parma hams showed that pressing before salting promotes the release of myofibrillar proteins, thus impacting proteolysis and dry-cured ham quality parameters (Paredi et al, 2017).

The effect of pressing before salting might also affect the concentration of proteins involved in dry-cured ham pigmentation, such as myoglobin (Paredi et al, 2017). While 95% of hemoglobin is removed upon bleeding and slaughter, myoglobin stays bright red as long as it stays within muscle fibers and receives enough oxygen from hemoglobin. If myoglobin is released upon pressing or if exposition to oxygen is too long, meat becomes dark and less appealing for consumers (Paredi et al, 2017; Stefanon et al, 2012).

Other common defects include skin lesions, tough spots, red skin and veining defects. All of them may result from pre-slaughter and slaughter procedures and can cause bacterial spoilage, thus causing tissue separation, larger hematomas and DFD meat (Candek-Potokar et al, 2012).

4.8.2. Microbiological profile

Research has shown that fresh pork meat contains a variety of bacteria that derive from animal skin or digestive tract, washing procedures and/or processing environment. The most prevalent bacteria are Pseudomonas, Acinetobacter, Micrococcus, Staphylococcus, Enterobacter, Flavobacterium, Microbacterium and Lactobacillus. Major pathogens, instead, include Listeria monocyctogenes, Salmonellae, Staphylococcus aureus and other sulphite-reducing clostridia. Hence, proper hygienic practices are key to prevent pathogens from growing (San Daniele ham consortium, 2014).

Among all pathogens found in dry-cured ham, Staphylococcus aureus, sulphite-reducing clostridia and Toxoplasma gondii, a toxoplasmosis-causing protozoa, do not represent a major threat for consumers compared to other pathogens described later on in this paragraph. Although 5x10^5-10^6 colony forming units (CFU) of Staphylococci per gram can cause human intoxication, refrigeration, high salt concentrations and the lower cut-off of 10^7 - 10^8 CFU/g help prevent bacterial contaminations (San Daniele ham Consortium, 2014). Similarly, dry-curing longer than 1 year, high salt concentrations and a_w lower than 0.92 inactivate Toxoplasma gondii oocysts (Bayarri et al, 2010; Herrero et al, 2017). Furthermore, although the transition from the cold phase (salting and resting) to the drying phase increases the risk of Escherichia Coli growth, prolonged resting can significantly reduce the risk (Merialdi et al, 2016).

Conversely, Listeria and Salmonellae represent a greater threat in the setting of dry-cured ham production as they can cause dangerous infections called listeriosis and salmonellosis, respectively. What is more, as Listeria monocyctogenes thrives in cold and moist locations, dry-cured ham produced according to strict hygienic standards can still be contaminated by Listeria when put into contact with contaminated meat slicers (San Daniele ham Consortium, 2014). After ingestion of contaminated ham, it takes between 1 and 4 weeks for symptoms to occur (CDC, 2017). Salmonella, instead, grows aerobically or anaerobically at
37°C (98.6°F) and at a pH of 6.5- 7.5. When contracted, salmonellosis provides GI symptoms within 12 to 72 hours. While less than 10 cells are needed to cause salmonellosis, high-fat foods may require lower infectious doses to cause the disease (AMSA, 2015).

According to the European Food Safety Authority and European Centre for Disease Prevention and Control (EFSA & CDC, 2014), there were respectively 91,034 and 1,642 confirmed human cases of salmonellosis and listeriosis in the European Union in 2012. These foodborne pathogens were mainly detected in meat and Ready-to-Eat (RTE) products of meat origin, where RTE was defined as “any food which is normally eaten in its raw state or any food handled, processed, mixed, cooked, or otherwise prepared into a form which is normally eaten without further listericidal steps” (FAO, 2005). Accordingly, the Commission Regulation (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for RTE foods established that *Listeria monocytogenes* must not exceed the limit of 100 CFU/g and that there should be no traces of *Salmonellae* in 25 g of product by the end of its shelf-life (EC, 2005). Conversely, in case of contamination, meat producers must contact veterinary inspectors and implement control measures and appropriate corrections to prevent any issues in the future (San Daniele ham Consortium, 2014). Nonetheless, several PDO ham producers apply “zero tolerance” policies to *Listeria* to minimize the human risk of contamination (see paragraph 5.4).

5. PDO HAM AND HUMAN HEALTH

Studying nutrient composition can help identify the foods dry-cured ham can be combined with to meet individual nutrition needs. In fact, aiming for a varied diet is the best choice to meet personal requirements and promote healthy aging (INRAN, 2003).

5.1. Nutrient composition of Italian PDO ham

5.1.1. Nutrient composition of Italian PDO ham compared to other Italian deli pork meats.

Figure 16 shows that the nutrition composition of San Daniele and Parma hams (both with or without visible fat removed) is similar in many respects. In fact, these food products provide more protein and cholesterol, and less calories and fat than *mortadella* (endowed with PGI recognition, Protected Geographical Indication) or *pancetta*. While *mortadella* is made from a mixture of lean muscle (mainly shoulder) and fat lardons from the throat area, *pancetta* is made from the front part of the ribs. *Salame (Milano)* instead, is a flavorful kind of salami made from pork shoulder. Overall, Figure 16 shows that *Salame (Milano)* provides more kcal, fat and cholesterol and less protein than San Daniele and Parma hams (ASSICA, 2013).

<table>
<thead>
<tr>
<th>Italian deli meat (50g portion)</th>
<th>Energy (kcal)</th>
<th>Protein (g)</th>
<th>Fat (g)</th>
<th>Cholesterol (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Daniele ham</td>
<td>136</td>
<td>12.9</td>
<td>9.3</td>
<td>41.5</td>
</tr>
<tr>
<td>San Daniele ham (visible fat removed)</td>
<td>88</td>
<td>14.5</td>
<td>3.3</td>
<td>45.5</td>
</tr>
<tr>
<td>Parma ham</td>
<td>135</td>
<td>13.0</td>
<td>9.2</td>
<td>40.5</td>
</tr>
<tr>
<td>Parma ham (visible fat removed)</td>
<td>88</td>
<td>14.6</td>
<td>3.2</td>
<td>44.5</td>
</tr>
<tr>
<td><em>Mortadella</em> (PGI)</td>
<td>144</td>
<td>7.9</td>
<td>12.5</td>
<td>36.0</td>
</tr>
<tr>
<td><em>Pancetta</em> (rolled up)</td>
<td>265</td>
<td>7.6</td>
<td>26.1</td>
<td>34.0</td>
</tr>
<tr>
<td><em>Salame</em> (Milano)</td>
<td>192</td>
<td>12.7</td>
<td>15.5</td>
<td>52.0</td>
</tr>
</tbody>
</table>

Figure 16: Calories, protein, lipid and cholesterol contents of 50 g of varied Italian deli meats (ASSICA, 2013)

With regards to fat content, the ratio between saturated and unsaturated fatty acids has decreased over the years in dry-cured ham so that the ratio now tends towards the typical values of vegetable oils or fish. For example, San Daniele ham contains 35% SFA and 65% PUFA while San Daniele ham deprived of visible
fat contains 33% SFA and 67% PUFA. In addition to that, 50 g of San Daniele contain 1.18 g of omega-6, which represent 13% of daily suitable intake %, 0.06 g ALA (omega-3) which represent 5% of suitable intake %, and 0.01 g of a mixture of EPA and DHA, which represent 5% of daily suitable intake % (ASSICA, 2013).

Like other Italian deli meats, Italian PDO ham is a source of minerals such as iron, zinc, sodium, potassium, phosphorus, magnesium and selenium, which play important biological roles in the human body (Figure 17).

<table>
<thead>
<tr>
<th>Mineral in Italian deli meats</th>
<th>Main biological roles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron (Fe)</td>
<td>cellular respiration, nucleic acid metabolism, collagen synthesis</td>
</tr>
<tr>
<td>Zinc (Zn)</td>
<td>growth, wound healing, taste and smell perception</td>
</tr>
<tr>
<td>Sodium (Na)</td>
<td>water retention, osmotic pressure</td>
</tr>
<tr>
<td>Potassium (K)</td>
<td>neuromuscular activity, heart contraction, acid-base balance, water retention, osmotic pressure</td>
</tr>
<tr>
<td>Phosphorus (P)</td>
<td>protein construction, energy utilization from food</td>
</tr>
<tr>
<td>Magnesium (Mg)</td>
<td>skeleton construction, activity of nerves and muscles, metabolism of fat and protein</td>
</tr>
<tr>
<td>Selenium (Se)</td>
<td>metabolism of thyroid hormones, protection from oxidative stress</td>
</tr>
</tbody>
</table>

Figure 17: Biological roles of minerals found in San Daniele ham and other Italian deli meats (ASSICA, 2013; Gropper et al, 2009)

Figure 18 compares the mineral composition of 50 g of several Italian deli pork meats. As evidenced in bold, dry-cured ham provides particularly high RDA % (Recommended Daily Amount %) of zinc, potassium and phosphorus. No RDA % has been set for sodium.

<table>
<thead>
<tr>
<th>Italian deli meat (50 g portion)</th>
<th>mg Iron (RDA%)</th>
<th>mg Zinc (RDA%)</th>
<th>mg Potassium (RDA%)</th>
<th>mg Phosphorus (RDA%)</th>
<th>mg Magnesium (RDA%)</th>
<th>mg Selenium (RDA%)</th>
<th>mg Sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Daniele ham</td>
<td>0.45 (3%)</td>
<td>1.2 (12%)</td>
<td>291 (15%)</td>
<td>92.0 (13%)</td>
<td>10.0 (3%)</td>
<td>7.0 (13%)</td>
<td>900</td>
</tr>
<tr>
<td>San Daniele ham (visible fat removed)</td>
<td>0.55 (4%)</td>
<td>1.35 (14%)</td>
<td>334 (17%)</td>
<td>105.5 (15%)</td>
<td>11.5 (3%)</td>
<td>8.0 (15%)</td>
<td>1020</td>
</tr>
<tr>
<td>Parma ham</td>
<td>0.45 (3%)</td>
<td>1.15 (12%)</td>
<td>269 (13.5%)</td>
<td>90 (13%)</td>
<td>10.0 (3%)</td>
<td>5.5 (10%)</td>
<td>880</td>
</tr>
<tr>
<td>Parma ham (visible fat removed)</td>
<td>0.50 (4%)</td>
<td>1.3 (13%)</td>
<td>309 (15%)</td>
<td>103.5 (15%)</td>
<td>11.5 (3%)</td>
<td>6.5 (12%)</td>
<td>1020</td>
</tr>
<tr>
<td>Mortadella</td>
<td>0.50 (4%)</td>
<td>0.80 (8%)</td>
<td>157 (8%)</td>
<td>59.5 (8%)</td>
<td>8.5 (2%)</td>
<td>10.0 (18%)</td>
<td>480</td>
</tr>
<tr>
<td>Pancetta, rolled up</td>
<td>0.20 (1%)</td>
<td>0.65 (6%)</td>
<td>185 (9%)</td>
<td>59.0 (8%)</td>
<td>6.0 (2%)</td>
<td>5.5 (10%)</td>
<td>600</td>
</tr>
<tr>
<td>Salame (Milano)</td>
<td>0.60 (4%)</td>
<td>1.50 (15%)</td>
<td>657 (16%)</td>
<td>328.5 (15%)</td>
<td>10.5 (3%)</td>
<td>8.0 (15%)</td>
<td>780</td>
</tr>
</tbody>
</table>

Figure 18: Mineral content of 50g of several Italian deli pork meats (ASSICA, 2013)

Figure 19 shows that both San Daniele and Parma hams are major sources of water-soluble vitamins like B1, B2, B3, B6 and B12. Vitamins B1, B2 and B3 (i.e. thiamine, riboflavin and niacin) protect nervous tissues, skin and mucous membranes and support the metabolism of carbohydrate, cellular
respiration and the synthesis and digestion of amino acids, fatty acids and cholesterol. Vitamin B6 is involved in the metabolism of nitrogen compounds and promotes the synthesis of hemoglobin and the metabolism of carbohydrates and lipids. Vitamin B12, instead, is involved in the metabolism of amino acids, fatty acids and nucleic acids and promotes red blood cell maturation, nerve function and hemoprotein synthesis. Its deficiency can cause pernicious anemia and lack of folic acid, another risk factor of anemia (Gropper et al, 2009).

All deli meats reported in Figure 19 contain traces of vitamin E too. This liposoluble vitamin is a natural antioxidant and its deficiency can lead to metabolic or neurological problems (Gropper et al, 2009).

<table>
<thead>
<tr>
<th>Italian deli meat (50 g portion)</th>
<th>B1 (RDA%)</th>
<th>B2 (RDA%)</th>
<th>B3 (RDA%)</th>
<th>B6 (RDA%)</th>
<th>B12 (RDA%)</th>
<th>Vitamin E (RDA%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Daniele ham</td>
<td>0.34 (31%)</td>
<td>0.10 (7%)</td>
<td>2.57 (16%)</td>
<td>0.52 (37%)</td>
<td>0.24 (9%)</td>
<td>0.07 (0.6%)</td>
</tr>
<tr>
<td>San Daniele ham (visible fat removed)</td>
<td>0.39 (35%)</td>
<td>0.12 (8%)</td>
<td>2.95 (18%)</td>
<td>0.60 (43%)</td>
<td>0.27 (11%)</td>
<td>0.08 (0.6%)</td>
</tr>
<tr>
<td>Parma ham</td>
<td>0.45 (41%)</td>
<td>0.11 (8%)</td>
<td>2.95 (18%)</td>
<td>0.57 (41%)</td>
<td>0.34 (14%)</td>
<td>0.11 (1%)</td>
</tr>
<tr>
<td>Parma ham (visible fat removed)</td>
<td>0.52 (47%)</td>
<td>0.13 (9%)</td>
<td>3.39 (21%)</td>
<td>0.65 (46%)</td>
<td>0.39 (16%)</td>
<td>0.11 (1%)</td>
</tr>
<tr>
<td>Mortadella</td>
<td>0.12 (11%)</td>
<td>0.06 (4%)</td>
<td>2.10 (13%)</td>
<td>0.14 (9%)</td>
<td>0.14 (6%)</td>
<td>0.04 (0.3%)</td>
</tr>
<tr>
<td>Pancetta, rolled-up</td>
<td>0.18 (17%)</td>
<td>0.03 (2%)</td>
<td>1.43 (9%)</td>
<td>0.03 (2%)</td>
<td>0.26 (10%)</td>
<td>0.12 (1%)</td>
</tr>
<tr>
<td>Salame (Milano)</td>
<td>0.53 (24%)</td>
<td>0.17 (6%)</td>
<td>4.97 (16%)</td>
<td>0.16 (11%)</td>
<td>0.56 (11%)</td>
<td>0.08 (0.7%)</td>
</tr>
</tbody>
</table>

Figure 19: Vitamin content of 50 g of several Italian deli pork meats (ASSICA, 2013)

5.1.2. Nutrient composition of Italian PDO ham compared to other foods

Figure 20 shows the nutrient composition of San Daniele ham and other foods. One hundred grams of San Daniele ham contain more protein than the same amount of pork steak, beef fillet and chicken breast. One hundred grams of dry-cured ham contain more protein and less cholesterol than the same amount of mackerel. Also, by removing visible fat, the SFA content of dry-cured ham decreases, thus getting closer to that of mackerel or canned tuna (drained). While meat and seafood are all major sources of iron and zinc, the table shows that San Daniele ham provides more potassium than many meat or seafood products. Moreover, one hundred grams of San Daniele ham provide more selenium than 100 g of many plant foods and more vitamin E than 100 g of grains.
<table>
<thead>
<tr>
<th>Food (100g)</th>
<th>kcal</th>
<th>Prot (g)</th>
<th>Fat (g)</th>
<th>SFA (g)</th>
<th>Chol (mg)</th>
<th>Fe (mg)</th>
<th>Zn (mg)</th>
<th>Mg (mg)</th>
<th>Na (mg)</th>
<th>K (mg)</th>
<th>Se (mcg)</th>
<th>Folic (mcg)</th>
<th>vit E (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Daniele ham</td>
<td>271</td>
<td>25.7</td>
<td>18.6</td>
<td>6.47</td>
<td>83</td>
<td>0.9</td>
<td>2.4</td>
<td>20</td>
<td>1800</td>
<td>581</td>
<td>14</td>
<td>2</td>
<td>0.13</td>
</tr>
<tr>
<td>S. Daniele ham (fat removed)</td>
<td>176</td>
<td>29.0</td>
<td>6.5</td>
<td>2.16</td>
<td>91</td>
<td>1.1</td>
<td>2.7</td>
<td>23</td>
<td>2040</td>
<td>667</td>
<td>16</td>
<td>2</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Meat and seafood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pork steak</td>
<td>157</td>
<td>21.3</td>
<td>8.0</td>
<td>3.66</td>
<td>62</td>
<td>0.8</td>
<td>1.6</td>
<td>17</td>
<td>56</td>
<td>290</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Beef fillet</td>
<td>127</td>
<td>20.5</td>
<td>0</td>
<td>1.67</td>
<td>2</td>
<td>1.9</td>
<td>2.8</td>
<td>20</td>
<td>41</td>
<td>330</td>
<td>17</td>
<td>10</td>
<td>0.12</td>
</tr>
<tr>
<td>Chicken breast</td>
<td>100</td>
<td>23.3</td>
<td>0.8</td>
<td>0.25</td>
<td>60</td>
<td>0.4</td>
<td>0.7</td>
<td>32</td>
<td>33</td>
<td>370</td>
<td>10</td>
<td>14</td>
<td>0.13</td>
</tr>
<tr>
<td>Mackerel</td>
<td>170</td>
<td>17.0</td>
<td>11.1</td>
<td>2.6</td>
<td>95</td>
<td>1.2</td>
<td>2.0</td>
<td>21</td>
<td>130</td>
<td>360</td>
<td>9.8</td>
<td>1</td>
<td>0.25</td>
</tr>
<tr>
<td>Tuna, canned (drained)</td>
<td>192</td>
<td>25.5</td>
<td>10.1</td>
<td>1.94</td>
<td>65</td>
<td>1.7</td>
<td>1.1</td>
<td>33</td>
<td>316</td>
<td>301</td>
<td>90</td>
<td>5</td>
<td>2.18</td>
</tr>
<tr>
<td><strong>Fruits and vegetables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lettuce</td>
<td>19</td>
<td>1.8</td>
<td>0.4</td>
<td>0.05</td>
<td>0</td>
<td>0.8</td>
<td>0.2</td>
<td>14</td>
<td>9</td>
<td>240</td>
<td>9</td>
<td>64</td>
<td>0.66</td>
</tr>
<tr>
<td>Tomato</td>
<td>19</td>
<td>1.0</td>
<td>0.2</td>
<td>0.03</td>
<td>0</td>
<td>0.3</td>
<td>0.1</td>
<td>10</td>
<td>6</td>
<td>297</td>
<td>2</td>
<td>15</td>
<td>1.06</td>
</tr>
<tr>
<td>Apple</td>
<td>53</td>
<td>0.3</td>
<td>0.1</td>
<td>0</td>
<td>0</td>
<td>0.3</td>
<td>0</td>
<td>4</td>
<td>2</td>
<td>125</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Orange</td>
<td>34</td>
<td>0.7</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
<td>0.2</td>
<td>0.2</td>
<td>10</td>
<td>3</td>
<td>200</td>
<td>0</td>
<td>31</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>Grains</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole wheat bread</td>
<td>224</td>
<td>7.5</td>
<td>1.3</td>
<td>&lt;0.30</td>
<td>0</td>
<td>2.5</td>
<td>1.6</td>
<td>0</td>
<td>550</td>
<td>210</td>
<td>0</td>
<td>39</td>
<td>0.2</td>
</tr>
<tr>
<td>Pasta</td>
<td>353</td>
<td>10.9</td>
<td>1.4</td>
<td>0.22</td>
<td>0</td>
<td>1.4</td>
<td>1.2</td>
<td>51</td>
<td>4</td>
<td>192</td>
<td>3</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>Rice</td>
<td>332</td>
<td>6.7</td>
<td>0.4</td>
<td>0.10</td>
<td>0</td>
<td>0.8</td>
<td>1.3</td>
<td>20</td>
<td>5</td>
<td>92</td>
<td>10</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Farro</td>
<td>335</td>
<td>15.1</td>
<td>2.5</td>
<td>0</td>
<td>0</td>
<td>0.7</td>
<td>0</td>
<td>0</td>
<td>18</td>
<td>440</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Dairy products</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk 2%</td>
<td>46</td>
<td>3.5</td>
<td>1.5</td>
<td>0.89</td>
<td>7</td>
<td>0.1</td>
<td>0.4</td>
<td>11</td>
<td>46</td>
<td>170</td>
<td>2</td>
<td>6</td>
<td>0.04</td>
</tr>
<tr>
<td>Low fat fruit yogurt</td>
<td>90</td>
<td>4.1</td>
<td>0.7</td>
<td>0.02</td>
<td>4</td>
<td>0.1</td>
<td>0.5</td>
<td>15</td>
<td>64</td>
<td>210</td>
<td>1</td>
<td>16</td>
<td>0.01</td>
</tr>
<tr>
<td>Mozzarella cheese</td>
<td>253</td>
<td>18.7</td>
<td>19.5</td>
<td>11.5</td>
<td>46</td>
<td>0.4</td>
<td>2.6</td>
<td>10</td>
<td>200</td>
<td>145</td>
<td>3</td>
<td>16</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Other plant foods</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walnuts, no shell</td>
<td>689</td>
<td>14.3</td>
<td>68.1</td>
<td>5.57</td>
<td>0</td>
<td>2.1</td>
<td>2.7</td>
<td>131</td>
<td>2</td>
<td>368</td>
<td>3</td>
<td>66</td>
<td>3.00</td>
</tr>
<tr>
<td>Chickpeas, canned</td>
<td>100</td>
<td>6.7</td>
<td>2.3</td>
<td>0.18</td>
<td>0</td>
<td>1.8</td>
<td>1.03</td>
<td>24</td>
<td>311</td>
<td>109</td>
<td>1</td>
<td>7</td>
<td>1.05</td>
</tr>
</tbody>
</table>

Figure 20: Nutrient composition of varied foods (prot = protein, carb = carbohydrates, leu = leucine, chol = cholesterol, Fe = iron, Zn = zinc, Mg = magnesium, Na = sodium, K = potassium, Se = selenium, folic = folic acid, vit E = vitamin E) (INRAN, 2000; IEO, 2008)
5.2. PDO ham intake in varied life stages

Dry-cured ham provides nutrients that are essential in varied life stages or settings.

5.2.1. Growth and development

Body growth, a hallmark of childhood and adolescence, is enhanced when the right amounts of protein and, other compounds, such as minerals and vitamins, are provided. A positive daily balance between protein input and output is key to build new body structures. Accordingly, children and adolescents require specific amounts of proteins to support growth and development (SINU, 2014) (Figure 21).

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Protein (g/kg/day) Population Reference Intake</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>1.00</td>
<td>50 grams of San Daniele ham provide 12.9 of protein.</td>
</tr>
<tr>
<td>4-6</td>
<td>0.94</td>
<td>A healthy male adolescent of 15 years of age, 170 cm of height and 62 kg of body weight needs 0.95g/kg, i.e. 59 g of protein a day</td>
</tr>
<tr>
<td>7-10</td>
<td>0.99</td>
<td>50 g of ham can provide 22% of his daily protein intake</td>
</tr>
<tr>
<td>11-14 (M)</td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td>11-14 (F)</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>15-17 (M)</td>
<td>0.95</td>
<td></td>
</tr>
<tr>
<td>15-17 (F)</td>
<td>0.90</td>
<td></td>
</tr>
</tbody>
</table>

Figure 21: Protein requirements in childhood and adolescence (Source: SINU, 2014)

Italian PDO ham is a source of leucine, an essential amino acid. For example, San Daniele ham provides 272 mg /100g. Leucine daily requirements are 54 mg/kg in children aged 1-2, 44 mg/kg in children aged 4-13, and 42 mg/kg in children aged 14-18 (Pencharz et al, 2006). More in detail, leucine promotes protein synthesis via mTOR (Young et al, 2013), a protein that phosphorylates eukaryotic initiation factor (eIF), 4E binding protein 1 (4E-BP1) and p70 ribosomal protein S6 kinase (p70S6k). Upon phosphorylation, 4E-BP1 promotes the formation of the eIF4F complex which allows 43S pre-initiation complex to bind the 5’ cap of most mRNAs and initiate translation. Then, phosphorylated p70S6k enhances the helicase activity of eIF4A, a component of eIF4F, which further accelerates the initiation of translation (You et al, 2015).

Among micronutrients for growth and development, ham’s iron, like iron from meat and fish, is more bioavailable than plant-derived iron. This is key considering that children, who often dislike fruits and vegetables, require iron for growth and iron-deficiency anemia is a major public health problem worldwide (Figure 20 and 22). In addition, thanks to its high zinc content, Italian PDO ham may help prevent growth delay caused by zinc deficiency (Figure 20 and 22). This is of public health importance considering that recommended zinc intake levels are not being reached by adolescents in the USA and the UK due to decreasing meat consumption (Jiménez-Colmenero et al, 2010) (Figure 22).
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Iron (mg/day)</th>
<th>Zinc (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>4-6</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>7-10</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>11-14 (M)</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>11-14 (F)</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>15-17 (M)</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>15-17 (F)</td>
<td>18</td>
<td>9</td>
</tr>
</tbody>
</table>

Figure 22: Iron and zinc requirements in childhood and adolescence (SINU, 2014)

Overall, a small sandwich made with whole grain bread and three slices of San Daniele ham contains more protein, iron, zinc, fiber and less sugar than a cookie-like snack full of SFA and trans fats (Figure 23).

<table>
<thead>
<tr>
<th>Portion</th>
<th>Kcal</th>
<th>Protein (g)</th>
<th>Leucine (mg)</th>
<th>Carbohydrates (g)</th>
<th>Lipids (g)</th>
<th>Fiber (g)</th>
<th>Iron (mg)</th>
<th>Zinc (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sandwich with San Daniele ham</td>
<td>50 g +50 g</td>
<td>248</td>
<td>16.7</td>
<td>136</td>
<td>24</td>
<td>10.0</td>
<td>3</td>
<td>1.70</td>
</tr>
<tr>
<td>Packaged, cookie-like snack</td>
<td>50 g</td>
<td>222</td>
<td>2.7</td>
<td>193</td>
<td>36</td>
<td>8.6</td>
<td>0</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Figure 23: Nutrient comparison between a whole grain sandwich with San Daniele ham and a packaged snack (ASSICA, 2013; IEO, 2008; INRAN, 2000)

5.2.2. Pregnancy and lactation
What a woman eats and drinks during pregnancy represents her baby’s main source of nourishment. Accordingly, mothers-to-be should consume small, frequent snacks that are rich in protein, and choose a variety of healthy foods and beverages. The goal is to provide the newborn with all of the other nutrients that can ensure proper growth and development (USDHHS, 2018; PDHU, 2018).

Italian PDO ham is a source of important nutrients for pregnant and lactating women such as protein, iron, zinc, potassium, magnesium, selenium and folate (Figures 20 and 24). Folate contributes to prevent megaloblastic anemia and defects in the neuronal tube and, like iron, folate is more bioavailable in meat than in fruits and vegetables (Biesalski, 2005).
On the other hand, pregnant women must pay special attention to food safety. If they get a foodborne illness, the health consequences on the newborn can be serious. For example, a fetus infected with *Listeria* or *Toxoplasma* can develop intellectual disability, paralysis, blindness and other impairments later in life (CDC, 2017; USDHHS 2018). This is why nutrition experts warn pregnant women against consuming raw foods that can carry bacteria (USDHHS, 2018; PDHU, 2018). In particular, the Italian Ministry of Health points out that deli meats cured for a short period of time, especially if homemade, are at higher risk of carrying *Toxoplasma, Listeria* and *E.Coli*. Conversely, one year of curing seems sufficient to inactivate *Toxoplasma gondii*'s cysts (Herrero et al; 2017; IZSV, 2017). Furthermore, as *Listeria* may be found on meat slicers and survive for some months after packaging (see paragraph 4.8.2), pregnant women who choose to consume deli meats should opt for refrigerated packaged products and heat the slices until-steaming hot soon after opening the package (IZSV, 2017). While these precautions are thought kill *Listeria* and make the product suitable for consumption during pregnancy or in the setting of immunodeficiency disorders (USDHHS, 2018; PDHU, 2018), heat can strongly affect meat flavor and denature peptides (Martinez Sanchez et al, 2017).

### 5.2.3. Active adulthood

Adults who regularly engage in physical activity or perform job duties that require physical exertion should drink at least 2 liters of water a day and eat highly digestible foods that are high in protein, low in fat and rich in micronutrients or other compounds that boost performance.

Two thirds of body weight is water in the average adult. Water serves as solvent and provides a means of transportation of compounds throughout the body. In the setting of physical activity, it helps excrete wastes, regulate blood volume and pressure, transports oxygen and nutrients to the brain and muscles and helps transfer heat out of the body via sweat. Humans usually notice they are dehydrated when they undergo hypovolemia (i.e. a decrease in the amount of water in their blood), hyperglycemia (i.e. an increase in blood sugar) or have a dry feeling in their mouth. Unfortunately, dehydration has been going on for a while when any of these symptoms occur (GSSI, 2018). In addition, active adults can lose up to 1,000-3,000 mg of sodium after a heavy 1-hour workout because 0.5 kg (about 1 lb) of sweat contains about 500-700 mg sodium. Therefore, adults who exercise for more than 1-2 hours in hot weather should choose salty foods and/or beverages before and after their workout sessions to help delay the rate of dehydration and enhance endurance. In particular, as shown in Figure 20, Italian PDO ham is rich in salt, especially when fat is trimmed (Ivanovic et al, 2016). While ¼ teaspoon of salt contains 600mg of sodium, 50mg of San Daniele ham contain 900mg of sodium and one glass of sport drink contains only 75mg of sodium (Clark, 2014; ASSICA, 2013) (Figure 25).
Active adults need 0.8g protein/kg of body weight. Almost half of our body is made out of protein, which helps ensure structure, movement, immune function, transport, hormones, enzymes and communication between and in-between cells. Consuming dietary amino acids is key as exercise leads to both protein breakdown and muscle protein synthesis and the human body doesn’t store amino acids as a source of protein synthesis. While some amino acids are made by the body, others are essential or conditionally essential as they become essential in certain conditions or diseases (Figure 25). Moreover, active individuals who ingest 45 mg of leucine/kg/day and 22.5 mg /kg/day of the other two branched-chain amino acids, isoleucine and valine, can promote muscle protein synthesis via mTOR pathway, mitochondrial biogenesis and reactive oxygen species scavenging. Thus, 50g of dry-cured ham provide not only more than a third of the protein needs of a 70 kg (154 lb) adult but also 60% of daily leucine needs and all essential amino acids (Blomstrand et al, 2006; Foure et al, 2017).

Research has shown that dry-cured ham may be also a source of carnosine, arnosine, L-carnitine, creatine, anserine and taurine. These compounds are thought to benefit active individuals in different ways. Carnosine and arnosine are two antioxidant histidyl-dipeptides particularly abundant in glycolytic muscles, which help fight inflammatory responses after physical activity and help prevent lipid oxidation in pork meat. L-carnitine plays a role in energy production, helps lower cholesterol levels and promotes chromium picolinate absorption thus facilitating the synthesis of lean mass. While creatine provides energy for vigorous mass contraction, anserine is a dipeptide known to buffer pH, thus increasing anaerobic performance capacity. Moreover, dry-cured ham is a source of coenzyme Q10 (CoQ10), a lipid soluble endogenous hydroxy-benzoquinone, and taurine, an essential amino acid that can conjugate bile acids and possibly protect against oxidative stress (Ivanovic et al, 2016; Marusic et al, 2013; Young et al, 2013). A recent study of Spanish dry-cured ham explored how the concentrations of all of these compounds changes over 10 months of processing. The study showed that free L-carnitine levels remained relatively stable at quite high levels (from 40.6 to 53.4 mg/100g dry matter), probably due to the conversion of carnitine esters to the free form. Concentrations of creatine decreased (from 1317.5 to dry 381.4mg/100g dry matter) while concentrations of creatinine increased during ham processing (from 11.6 to 331.7mg/100g of dry matter). In particular, the creatinine-to-carnitine ratio was higher in Semimembranosus muscle than in Biceps femoris, probably because the former is more exposed to temperature and humidity than the latter. Moreover, a decrease in carnosine and an increase in anserine concentrations were noted only between 3.5-5 months since the beginning of the curing process. Similarly, the levels of taurine in Biceps femoris increased from 23.2 to 212 mg/100g during dry-curing, indicating that dry-cured ham is a great source of taurine. Concentration of CoQ10, instead, decreased during curing but remained high (from 25.8 to 10.2 mg/100g dry matter) (Marusic et al, 2013).

5.2.4. Athletes

Athletes’ hydration and nutrition goals differ prior to, during and after training (GSSI, 2018).

The goal of hydrating prior to exercise is to start physical activity with a normal level of hydration and plasma electrolyte levels. It also allows sufficient time for urine output to get back to normal prior to the training event, which is particularly important in hot weather. In this regard, the Institute of Medicine (IOM) provided general guidance on the composition of sports beverages for individuals who practice prolonged physical activity in hot weather. According to IOM, beverages should contain about 20–30 meq/l sodium (chloride as the anion) (460-690mg/l), about 2–5 meq/l (78-195) potassium and ~5–10% carbohydrates. Individual carbohydrate and electrolyte needs depend on exercise intensity and duration as well as weather conditions. While carbohydrates provide energy, sodium and potassium help replace sweat electrolyte losses and sodium alone helps stimulate thirst. These components can be consumed in the form of fluids, gels, energy bars and other foods (ACEND, 2016; ACSM, 2007). Therefore, not only sport

<table>
<thead>
<tr>
<th></th>
<th>Energy (kcal)</th>
<th>Carbohydrates /Sugar (g)</th>
<th>Protein (g)</th>
<th>Sodium (mg)</th>
<th>Potassium (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>¼ teaspoon of salt</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>600 mg</td>
<td>0</td>
</tr>
<tr>
<td>Sport drink (100ml)</td>
<td>24</td>
<td>5.9</td>
<td>0</td>
<td>52 mg</td>
<td>12 mg</td>
</tr>
<tr>
<td>San Daniele ham (50g)</td>
<td>136</td>
<td>0.1</td>
<td>12.9</td>
<td>900 mg</td>
<td>291 mg</td>
</tr>
</tbody>
</table>

Figure 25: Comparison between a sport drink and San Daniele ham (ASSICA, 2013; Nutrition Label of Gatorade Ready-to-drink, Italy, 2018)
beverages but also salted foods like dry-cured ham can help athletes to ingest adequate sodium before exercising in the heat.

Consuming sodium during exercise helps maintain blood sodium concentration and fluid retention, thus preventing urination. In fact, total body water can be divided into two compartments: the intracellular space including water within muscle cells, and the extracellular space, including fluid in the space between cells and plasma. When plain water is consumed, water dilutes blood sodium concentration, the kidney turns off the signal to reabsorb water and urine is more watery. As soon as plasma sodium levels fall below 130 mEq/l (130 mmol/l), symptoms of hyponatremia such as bloating, weight gain, nausea, vomiting, headache and loss of consciousness, can occur. On the contrary, sodium-containing beverages increase blood sodium concentration with the opposite effect (GSSI, 2018). Regardless, the source of sodium intake during exercise depends on the kind of sport and what is conveniently available during a training session, match or race.

After exercise, the goal is to fully replace any fluid and electrolyte losses via sport beverages and salty foods. While the ratio between ingested fluids and sweat losses should be 1:1 during exercise, the ratio can be 1.5:1 during recovery in order to account for continued sweating and post-training urination (GSSI, 2018). Hyponatremia is most common among slow competitors in triathlons and ultra-marathon races and may depend on sodium loss in sweat as well as high intakes of water or other low sodium drinks (Jeukendrup, 2011). Unfortunately, hyponatremia related to large sweating (>1.2 L/h), salty sweat, exercise exceeding 2 hours in duration and/or poor acclimatization to the environment can lead to exercise-induces cramps. In fact, although cramps generally dissipate before they can be studied in a spontaneous environment, they most frequently occur in muscles that are fatigued, hyperthermic and dehydrated (ACEND, 2016). These conditions are thought to impair muscle contractions while stretching, massaging, proper hydration, higher salt intake and pungent foods seem to provide relief, possibly through an inhibitory neural reflex that decreases activity in the cramping muscle (Clark, 2014).

After hydration, integrating carbohydrates and protein prior to the next training session is athletes’ second dietary priority. Protein requirement are generally 1.2-1.7g/kg for team athletes, 1.2-1.4g/kg for endurance athletes, 1.6-1.7g/kg for strength athletes and 1.5-1.7g/kg for power athletes. As 20 g of complete protein from egg or whey have been shown to stimulate muscle protein synthesis after exercise, researchers estimate that athletes need about 0.25 g of protein/kg while excess amino acids are oxidized or excreted. In other words, there is a plateau as to how much protein the muscle can use to promote protein synthesis at one time. In addition, although research regarding the so-called “recovery window”, i.e. 30-60 minutes after exercise, has been debated, increasing evidence has shown that the muscle is sensitive to protein intake for 24 hours post exercise. The earlier one starts eating protein after training, the more regular his/her protein intake pattern will be during the day (GSSI, 2018). Thus, dry-cured ham can be an ideal food to consume on active days.

All in all, as anticipated for active adults, athletes who work out in hot environments can easily consume plenty of electrolytes in their pre- and post-exercise meals. Although many sport drinks are available nowadays, sport drinks are good for taste and fluids rather than for electrolytes. Conversely, dry-cured ham provides both salt and high-quality protein.

5.2.5. Aging and sarcopenia

With age, teeth and gums become slightly more vulnerable to decay and infection, bones become more susceptible to fracture and muscles lose strength and flexibility due to an imbalance in protein turnover (Young et al, 2013). Although the mechanisms behind these phenomena are still unclear, it has been noted that satellite cells, which normally promote muscle regeneration, are lower in old adults. The progressive loss of muscle mass is called sarcopenia and can be exacerbated by simultaneous inflammation and related diseases (Figure 26) (Witham et al, 2008). Considering that physiological impairments prevent old adults from eating foods that require lots of chewing, such as meat, and performing daily living activities, such as grocery shopping, this population should practice resistance training and consume about 1 g of highly digestible protein per kg of body weight. Hence, Italian PDO ham would be an ideal food for old adults since it is easy to chew, rich in digestible protein and peptides, and fresh slices can be refrigerated for a few days.
Studies revealing the anti-oxidant potential of peptides found in PDO ham suggest that they may help prevent chronic diseases related to oxidative damage and old age, such as Alzheimer’s disease (Marusic et al, 2013). In addition, Marusic et al (2013) found that cysteine, reduced glutathione and, partially, carnosine derived from Spanish dry-cured ham have ACE-inhibiting activity. The researchers extracted peptide fractions and conducted experiments in Caco-2 cells, showing that the concentration inhibiting 50% of ACE activity (IC50 value) was 0.03mM for glutathione, 0.12mM for cysteine and 1.5mM for carnosine. Although the direct effect of glutathione on ACE activity was not noted in vivo, the researchers concluded that dry-cured ham contains ACE-inhibiting compounds that may counteract the negative effects of salt on blood pressure (Marusic et al, 2013).

Last but not least, it has been hypothesized that the anti-hypertensive compounds found in dry-cured ham may positively impact muscle accretion in the setting of age-related sarcopenia. In this regard, Witham et al (2008) noticed that hypertensive patients taking ACE inhibitors had greater cross-sectional muscle mass and a slower decline in walking speed than those taking other anti-hypertensive medications. Therefore, these authors tested perindopril, an ACE inhibitor medication, on older patients aged 65 years and over and affected by impairment of daily activities, finding an increase in muscle performance 20 weeks after treatment initiation (Witham et al, 2008).

5.3. Evidence supporting PDO ham intake in varied health conditions

Many chronic diseases are related to each other; in fact, obesity predisposes to dyslipidemia. Dyslipidemia can progress to atherosclerosis, and insulin resistance and inflammation can further link obesity to atherosclerosis (Figure 27). Altogether, these mechanisms suggest that a well-balanced dietary pattern that (1) limits energy intake, (2) prevents alterations in glucose and lipid metabolism and (3) reduces oxidative stress, may help combat the burden of chronic diseases (Anderson et al, 2014). Although high salt content does not make dry-cured meat intake advisable in the setting of hypertension, dry-cured meat may still have other properties that could help individuals with chronic diseases meet their own needs.

5.3.1 Overweight and obesity

WHO estimates that more than 1 billion people worldwide were overweight (BMI ≥ 25) and more than 300 million were obese (BMI ≥ 30) in 2005. Globally, 44% of diabetes burden, 23% of ischaemic heart disease burden and 7–41% of cancer burden can be attributed to overweight and obesity (WHO, 2009b).

General nutrition recommendations for weight loss include small frequent meals throughout the day, with protein at each. Not only spreading calories throughout the day helps regulate food intake and limits blood sugar lows, a major cause of cravings and weight gain, but also protein is the most satiating macronutrient (Chambers et al, 2015). Protein affects diet-induced thermogenesis and GI hormonal signalling and induces a sense of satiation and satiety due to a sensory experience of fullness soon after
ingestion (Figure 28) (Chambers et al, 2015).

*In vitro* experiments conducted on enteroendocrine epithelial cells have shown that meat protein hydrolysates induce the release of glucagon-like-peptide 1 (GLP-1), an incretin that reduces food intake and regulates appetite. Similarly, duodenal infusion experiments in rats have indicated that the same hydrolysates induce the release of cholecystokinin (CCK), a major gut-produced peptide hormone that increases satiety (Steinert et al, 2011; Young et al, 2013). Among human studies, Martinez-Gonzalez et al (2009) assessed the incidence of cardiovascular disease and weight gain for a minimum of 6 years in 13,293 healthy Spanish university graduates. After comparing the health status of the participants who ate 50g of Spanish dry-cured ham 4-times a week to those who ate the same portion once a week, the authors did not find any association between dry-cured ham intake and cardiovascular diseases or weight gain. Therefore, dry-cured ham does not seem to predispose to overweight or obesity according to these data (Martinez Gonzalez et al, 2009).

Besides protein, dry-cured ham is also source of thiamine, a water-soluble vitamin that acts as a cofactor in various enzymatic reactions affecting appetite (Mulvihil, 2004). Unfortunately, no studies have yet established the extent to which this vitamin may help regulate appetite and prevent weight gain in individuals consuming a moderate amount of dry-cured ham.

5.3.2 Cardiovascular disease

Cardiovascular disease is the leading cause of human mortality and complications worldwide (Young et al, 2013). Diet, genetics and environmental factors are all risk factors of cardiovascular disease. Contrary to genetics, however, diet is a modifiable risk factor. Consequently, dry-cured ham consumption may be tailored to one’s unique needs and prognosis.

Dry-cured ham is a source of SFA such as palmitic acid (25%), stearic acid (12%) and myristic acid (1.5%), which can raise total cholesterol, low-density lipoprotein (LDL) and reduce high-density lipoprotein (HDL), thus promoting atherosclerosis (i.e. the narrowing of the arteries caused by a buildup of plaque). On the other hand, dry-cured ham contains MUFA and PUFA, which are known to reduce LDL. Such heterogeneous fat composition seems hard to interpret at first glance. Nevertheless, published research has established that the ratios PUFA-to-SFA and omega-6-to-omega-3 PUFA can help predict cardiovascular impact. More in detail, dry-cured ham’s PUFA-to-SFA ratio is 0.17-0.35, which is lower than recommended (i.e. 0.4 or higher). Similarly, its omega-6-to-omega-3 ratio is typically 4 or higher, which is slightly above the recommended range. While these numbers indicate that the fatty acid profile of dry-cured ham does not meet the recommendations, other data suggest that it is a major source of omega-3 long chain PUFA, which fight inflammation (Jiménez-Colmenero et al, 2010).
To assess the effect of dry-cured ham on cardiovascular disease development, Garcia Rebollo et al. (1998) studied MUFA intake in 19 post-menopausal women who were prescribed two consecutive 6-week diets rich in oleic acid (22% of energy intake). In the first diet, oleic acid came from olive oil and acorn-fed Iberian ham while, in the second diet, it came from olive oil only. The researchers noticed a significant decrease in plasma total cholesterol, triglycerides and LDL in old adults consuming a diet including acorn-fed Iberian ham and olive oil while their levels stayed the same after eating the second one. Although researchers could not isolate the effect of MUFA from that of other dietary components, this study showed that a source of SFA like dry-cured ham does not necessarily represent a risk factor for cardiovascular disease (Garcia Rebollo et al., 1998). Similar results were obtained by Mayoral et al. (2003), who administered a 6-week diet replacing 120 g of meat with 120 g of acorn-fed Iberian ham to 13 males and 8 females with cardiovascular disease and an average age of 71. The diet was both preceded and followed by a basal diet period of 6 weeks. The researchers noticed that acorn-fed Iberian ham in the diet increased blood antioxidant substances, reduced mean arterial blood pressure and decreased lipid peroxidation compared to meat (Mayoral et al., 2003).

Some studies have led to the hypothesis that certain dry-cured ham components may prevent cardiovascular disease. As shown in paragraph 4.7.1., dry-cured ham contains peptides that may have ACE-inhibiting properties. Evidence has shown that food-derived ACE-inhibitors have a higher affinity to living tissues and are eliminated more slowly than ACE-inhibiting medications. For example, Zhang et al. (2010) treated normotensive rats with L-nitro-L-arginine methyl-ester (L-NAME) to cause systemic hypertension and then fed the rats with chicken collagen hydrolysates. The researchers noticed a significant increase in nitric oxide (NO, a vasodilator) and a significant decrease in blood soluble intercellular adhesion molecule-1 (ICAM, a biomarker of endothelial damage) one hour post-treatment as well as a significant decrease in blood pressure 8 weeks later. Although in vivo studies do not necessarily represent human physiology, this study suggest that protein hydrolysates may have a positive prognostic role owing to their ACE inhibitory activity and regulation of NO and ICAM (Figure 29) (Zhang et al., 2010). As for micronutrients, dry-cured ham contains magnesium and potassium, which help proper heart contraction, and folate, which helps control the levels of homocysteine, a biomarker of cardiovascular disease. These features indicate that dry-cured ham consumption may contribute to reduce cardiovascular disease risk (Jiménez-Colmenero, 2010).

5.3.3 Inflammation and cancer

The mediators of inflammation, primarily adhesion molecules and cytokines, are all induced by oxidative stress, a disturbance in the balance between free radicals and cellular antioxidant defenses. Oxidative stress is one of the causes of cancer and can be of two types: endogenous or exogenous (i.e. derived from pollutants, drugs, smoke, radiation) (Anderson et al., 2014). Similarly, dry-cured ham can be a source of both endogenous and exogenous antioxidants. While ubiquinone, vitamin C, carnosine and
arnosine are considered as endogenous antioxidants, selenium can be both endogenous and exogenous as it can be added to pork feed via sodium selenite or selenium-rich yeast. Interestingly, selenium intake is declining in Europe and reaching inadequate levels in some cases (Biesalski, 2005). These data suggest that dry-cured ham may contain antioxidants that may counteract the potential carcinogenicity of processed meats and help prevent selenium deficiency (Figure 30).

![Antioxidant peptides (at least in dry-cured ham)](Processed meat) → ? \[Carcinogenic compounds\] → Cancer

Figure 30: Representation of how dry-cured ham could help inhibit carcinogenesis in the context of processed meat and carcinogenesis.

Human studies suggest also that dry-cured ham could help fight inflammation by improving the crosstalk between pro-inflammatory platelets and monocytes and preventing monocyte adhesion to blood vessels. Conversely, a crossover study compared the effects of dry-cured ham and cooked ham in 38 healthy volunteers with systolic blood pressure higher than 125 mmHg. Compared to the intake of 100 g/day cooked ham for 4 weeks (which was used as control due to lack bioactive peptides in cooked ham), eating 80g of dry-cured a day for more than 11 months was associated with decreased pro-inflammatory P-selectin expression on platelets and reduced expression of several pro-inflammatory markers in circulating monocytes. Conversely, increased expression of integrin α4 receptor (VCAM-1R) and CXCR4 (SDF1 receptor) was higher in multiple subtypes of monocytes. Considering that other studies had found that the expression of VCAM-1R and CXCR4 is higher in healthy volunteers compared to individuals with coronary artery disease (CAD), this study suggests that dry-cured may have important cardiovascular benefits. On the other hand, the participants enrolled in this study were healthy volunteers, which prevents the generalization of the results to other populations (Martinez-Sanchez et al, 2017).

5.3.4 Type 2 diabetes

Changes in diet and reductions in physical inactivity levels increase insulin-resistance, a major cause of persistent hyperglycemia and a hallmark of type 2 diabetes. Accordingly, 6% of deaths are due to high blood glucose (WHO, 2009).

Observational studies indicate that consumption of animal protein products, mainly processed meat, may be associated with type 2 diabetes. However, results are inconsistent (USDA, 2015) as it is unclear whether meat from different animals can affect diabetes development or progression (Stettler et al, 2013).

To further clarify the relationship between meat intake and type 2 diabetes, a meta-analysis of eight studies found that the insulin and glucose responses caused by pork meat intake were similar to those caused by beef, chicken, shrimp, or a mixed source of protein. In three out of eight studies, pork was consumed only in the form of fresh cooked meat, in one study pork was consumed as processed meat only and in the other four studies, pork was consumed in both forms. This meta-analysis showed that, compared to eggs, processed pork led to a larger insulin response while there were no differences in glucose response in non-obese subjects. Instead, processed pork led to a lower insulin response and a higher glucose response compared with whey protein (Stettler et al, 2013).

Altogether, large, long-term epidemiologic studies are needed to thoroughly investigate any diabetogenic effects of processed meat and/or dry-cured ham. These studies may help clarify whether such effects are due to the presence of additives, such as sugar, in processed meat. If so, the likelihood that additive-free PDO ham products could alter one’s blood glucose profile or insulin-resistance would be much
5.3.5 Other diseases: osteoporosis and intestinal disease

**Osteoporosis**

Osteoporosis is a bone disease that can be prevented with regular physical exercise and adequate intake of protein, calcium and vitamin D but can be exacerbated by SFA, which impair calcium absorption. Although dairy foods have been described as the best foods for bone health, dry-cured ham is a source of magnesium and L-carnitine which promote calcium absorption thus counteracting the effect of SFA (Ivanovic et al, 2016). Considering that dry-cured ham is a source of collagen and that collagen provides the building blocks required for bone renewal, further research should also investigate whether pork collagen can positively impact bone health. In this regard, a recent study indicated that collagen hydrolysates from chum salmon can positively impact the viability and proliferation of human fetal osteoblasts (Fu et al, 2013).

A systemic review compared the impact of meat- or fish-derived proteins on bone mineral disease and fractures risk. Positive effects on bone were found in 3% of participants with a meat-containing diet and in 12% of individuals with a fish-containing diet while negative effects on bone were observed in 47.9% with a meat-containing diet and 2.7% of participants with a fish-containing diet. This study showed also that the most negative health effects occurred in subjects who were not following a Mediterranean way of eating (92.7%) (Perna et al, 2017). Altogether, data suggest that overall diet pattern may be a better predictor of health outcomes rather than single nutrients. Although more research is needed to address the role of dry-cured ham in the Mediterranean diet, a recent systemic review supported these data indicating a positive correlation between bone health and adherence to the Mediterranean diet (Savanelli et al, 2017).

**Intestinal disease**

Meat contains nucleotides that promote the growth, differentiation and maturation of enterocytes, a cell type with limited capacity for nucleotide synthesis (Rodriguez-Serrano et al, 2010). In particular, dietary nucleotides increase the synthesis of mucosal protein and the length of the villi in the small intestine, thus benefiting intestinal health in many respects (Young et al, 2013). Recent data have also shown that pork meat may positively affect the composition of gut bacteria, one of the major determinants of intestinal and overall health. Zhu et al (2015) compared the composition of gut bacteria in the caecum of rats upon sequencing the V4-V5 region of 16S rRNA gene. The rats were fed with proteins from red meat (beef and pork), white meat (chicken and fish) and other sources (casein and soy). While the structure of caecal bacterial communities did not differ among groups, rats fed with meat proteins and casein had significantly lower levels of pro-inflammatory lipopolysaccharide-binding proteins. Although more research is needed, these data suggest that meat proteins may benefit intestinal health while preventing inflammatory responses in the host (Zhu et al, 2015).

6. SAN DANIELE HAM: A PDO HAM OF EXCELLENCE

San Daniele ham is made in San Daniele del Friuli, an Italian village in the province of Udine, in Friuli Venezia Giulia region. It has owned a PDO since 1996. Such recognition demonstrates the link between the place and the product making sure that the rights of both San Daniele ham producers and consumers are valued and protected.

6.1 San Daniele ham production: from the pigs rearing to consumers’ table

To make San Daniele ham, pigs with industrial genotypes (Landrace and Large White) are bred with pigs with Duroc genotypes, thus obtaining carcasses with light marbling, proper yield for commercial purposes and lean mass percentage. Although the animals are raised and slaughtered in multiple Italian regions (i.e. Friuli-Venezia Giulia, Veneto, Lombardy, Piedmont, Emilia Romagna, Umbria, Tuscany, Marche, Abruzzi and Lazio), the final product is exclusively obtained in San Daniele del Friuli. Feeding ensures moderate daily growth, always referring to the production of carcasses included in the central classes of
European Economic Community Classification (EUROP). Pig shelters are well insulated and ventilated, allowing proper temperature and elimination of noxious gases. Flooring is minimally slatted and made out of hydro-repellent and anti-slippery materials while equipment is corrosion-resistant. At slaughter, pigs weigh at least 160 kg (353 lb) and are at least 9 months old (Gaspardo et al, 2007; MIPAAF, 2007; Toldrà et al, 2014).

After slaughter, pig thighs are selected and suspended in ventilated and refrigerated rooms for 24-36 hours. After trimming both fat and hide, salt is manually applied once a week for a month. After that, washing, brushing and drying procedures at or below 15° C are implemented and thighs are assessed for flaws. Then, they are coated with a mixture of flour, lard, water, and pepper and aged for 1-2 years. During this time frame, humidity is 57-63%, the ratio between sodium chloride and humidity is 7.8-11.2 and the proteolytic index (calculated as 100×non-protein nitrogen/total nitrogen) is 31 at maximum (MIPAAF, 2007; Toldrà et al, 2014). By the time curing ends, hams have lost up to 30% of their weight so that the final weight is between 7.5-10kg (16.5 – 22 lb) (MIPAAF, 2007; Toldrà et al, 2014).

The long curing process prevents the survival of *Toxoplasma gondii’s* oocysts. Moreover, if hams get contaminated by *Listeria or Salmonellae*, San Daniele ham producers segregate them to prevent further contamination. To further reduce the risk of *Listeria*, San Daniele ham producers apply the stricter limit of “no traces of *Listeria* every 25g” proposed by EN/ISO 11290-1. Regardless, experiments have shown that *Listeria* cannot multiply in San Daniele ham at 3-8 °C (37.8-46.4°F) or 20°C (68°F) and a_w values of 0.93. In addition, experiments conducted on hams destined to USA market (which requires stricter microbiological precautions) have shown that a salt percentage of 5.82 and an a_w value of 0.90 do not allow the proliferation of *Salmonellae* (MIPAAF, 2007).

From a nutritional standpoint, the lipid content of San Daniele ham has decreased by 19% in the previous years due to an overall decrease in SFA as well as a decrease in the ratio between saturated and unsaturated fats (Figure 31). These data show how San Daniele ham producers care about consumers’ health.

<table>
<thead>
<tr>
<th>Years</th>
<th>SFA in San Daniele ham</th>
<th>SFA/unsaturated fats in San Daniele ham</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>g/100g</td>
<td>Reduction % (1993-2011)</td>
</tr>
<tr>
<td>1993</td>
<td>7.56</td>
<td>-14%</td>
</tr>
<tr>
<td>2011</td>
<td>6.47</td>
<td></td>
</tr>
</tbody>
</table>

Figure 31: Comparison of San Daniele ham’s fat composition in 1993 and 2011 (ASSICA, 2013)

Overall, San Daniele ham can be freshly sliced or purchased in the form of ready, pre-sliced, diced or vacuum-packed products (San Daniele ham Consortium, 2014). Consumers can recognize San Daniele ham at first glance as it is shaped like a guitar with a 15 mm white fat layer on the outer leg, a pink-red lean part with some veining and the typical hoof in the end (Figure 32). Its taste is unique due to several factors too. For example, the length of curing, the development of alcohols, aldehydes and other compounds, and higher altitudes and drier air of Friuli Venezia Giulia provide sweetness and a stronger aftertaste (Toldrà et al, 2014, MIPAAF, 2007).

Figure 32: Picture of San Daniele ham (Retrieved from San Daniele ham Consortium website, 2014)
6.2 Sample one-day menus including San Daniele ham

As stated in paragraph 2.3, Italian Dietary guidelines state that healthy individuals can consume dry-cured ham about 2 times a week (URSANU, 2015). Using San Daniele ham as a case in point, the following three 1-day menus represent practical examples of how dry-cured ham can be incorporated into a healthy diet. Nonetheless, none of these menus is meant to replace personalized nutrition advice by health professionals.

Sample 1-day menu for childhood (2,300 kcal)

The 1-day menu shown in Figure 33 provides about 2,300 kcal in the form of carbohydrates (55% total kcal), protein (19% total kcal) and fat (26% total kcal). It also provides 7.9 % fat kcal from SFA, 224 mg of cholesterol and 25g of fiber. Among micronutrients, it provides about 1,213 mg of sodium, 5,174 mg of potassium, 11 mg of iron, 10 mg of zinc, 847 mg of calcium and 364 mg of magnesium. In this example, San Daniele ham is offered as part of a sandwich during school recess, with the goal to replace unhealthy packaged snacks. While ham could be offered twice a week, other snacks such as a yogurt or dried fruit could help lower a child’s weekly sodium intake.

<table>
<thead>
<tr>
<th>Meal</th>
<th>Food/ingredient</th>
<th>Amount (g/ml or other units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>Milk, 2% fat</td>
<td>200 ml (7 fl. oz)</td>
</tr>
<tr>
<td></td>
<td>Breakfast cookies (frollini)</td>
<td>60 g (2oz)</td>
</tr>
<tr>
<td></td>
<td>Strawberries</td>
<td>200 g (7oz)</td>
</tr>
<tr>
<td>Morning snack</td>
<td>No-salt bread</td>
<td>50 g (1.8oz)</td>
</tr>
<tr>
<td></td>
<td>San Daniele ham</td>
<td>40 g (1.4 oz)</td>
</tr>
<tr>
<td></td>
<td>Lettuce leaves</td>
<td>100 g (3.5 oz)</td>
</tr>
<tr>
<td>Lunch</td>
<td>Pasta</td>
<td>80 g (2.8 oz) (dry)</td>
</tr>
<tr>
<td></td>
<td>Tomatoes, ripe</td>
<td>200 g (7oz)</td>
</tr>
<tr>
<td></td>
<td>Meat sauce (lean beef)</td>
<td>20 g (2 tablespoons)</td>
</tr>
<tr>
<td></td>
<td>Extra virgin olive oil</td>
<td>15 g (1.5 tablespoons)</td>
</tr>
<tr>
<td></td>
<td>No-salt bread</td>
<td>80 g (2.8 oz)</td>
</tr>
<tr>
<td>Afternoon snack</td>
<td>Fruit yogurt</td>
<td>125 g (4.4 oz)</td>
</tr>
<tr>
<td></td>
<td>Banana</td>
<td>150 g (1 medium fruit)</td>
</tr>
<tr>
<td>Dinner</td>
<td>Chicken breast</td>
<td>180 g (6.3 oz)</td>
</tr>
<tr>
<td></td>
<td>Vegetable puree made with cauliflower, potato and parmesan cheese</td>
<td>100 g + 250 g + 15 g (3.5 oz + 8.8 oz + 0.5 oz) respectively</td>
</tr>
<tr>
<td></td>
<td>Extra virgin olive oil</td>
<td>15 g (1.5 tablespoons)</td>
</tr>
</tbody>
</table>

Figure 33: Sample 1-day plan for childhood (2,300 kcal) (INRAN, 2000; IEO, 2008)

Sample 1-day plan for a moderately active adult (2,800 kcal)

The 1-day menu shown in Figure 34 provides about 2,800 kcal in the form of carbohydrates (55% total kcal), protein (18% total kcal) and fat (27% total kcal). It also provides 2,052 mg of sodium, 4.6% fat kcal from SFA, 185 mg of cholesterol and 31 g of fiber. In this example, San Daniele ham is offered at dinner, after an intense training session in the heat. Its high sodium content can replenish sodium losses occurred with sweat. In addition to these benefits, this 1-day menu provides also 894 mg of calcium, 4,573 mg of potassium, 17 mg of iron, 13 mg of zinc and 100 mg of selenium.
<table>
<thead>
<tr>
<th>Meal</th>
<th>Food/ingredient</th>
<th>Amount (g/ml or other units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>Milk, 2% fat</td>
<td>200 ml (7 fl. oz)</td>
</tr>
<tr>
<td></td>
<td>Muesli</td>
<td>80 g (2.8 oz)</td>
</tr>
<tr>
<td></td>
<td>Orange juice, freshly squeezed</td>
<td>200 ml (7 fl. oz)</td>
</tr>
<tr>
<td>Morning snack</td>
<td>Banana</td>
<td>150 g (1 medium fruit)</td>
</tr>
<tr>
<td>Lunch</td>
<td>Brown rice</td>
<td>90 g (3 oz)</td>
</tr>
<tr>
<td></td>
<td>Chicken breast</td>
<td>100 g (3.5 oz)</td>
</tr>
<tr>
<td></td>
<td>Spinach</td>
<td>100 g (3.5 oz)</td>
</tr>
<tr>
<td></td>
<td>Extra-virgin olive oil</td>
<td>20 ml (2 tablespoons)</td>
</tr>
<tr>
<td></td>
<td>No-salt bread</td>
<td>80 g (2.8 oz)</td>
</tr>
<tr>
<td>Afternoon snack</td>
<td>Low fat fruit yogurt</td>
<td>125 g (4.4 oz)</td>
</tr>
<tr>
<td></td>
<td>Walnuts, shell removed</td>
<td>30 g (3 tablespoons)</td>
</tr>
<tr>
<td>Dinner</td>
<td>Pasta</td>
<td>90 g (3oz) (dry)</td>
</tr>
<tr>
<td></td>
<td>Canned tuna, oil removed</td>
<td>80 g (2.8 oz)</td>
</tr>
<tr>
<td></td>
<td>San Daniele ham</td>
<td>50 g (1.8 oz)</td>
</tr>
<tr>
<td></td>
<td>No-salt bread</td>
<td>70 g (2.5 oz)</td>
</tr>
<tr>
<td></td>
<td>Extra-virgin olive oil</td>
<td>10 ml (1 tablespoon)</td>
</tr>
<tr>
<td></td>
<td>Artichoke</td>
<td>200 g (7 oz)</td>
</tr>
</tbody>
</table>

Figure 34: Sample 1-day plan for an active adult (2,800 kcal) (INRAN, 2000; IEO, 2008)

Active adults who exercise in the afternoon could also consume dry-cured ham as part of their lunch, 2-3 hours prior to the workout. In this case, the goal would be to promote adequate sodium intake prior to the training session and to provide highly digestible protein to prevent GI overload. On the other hand, a high pre-workout sodium content would require particular attention to proper and regular hydration. Last but not least, based on the evidence reported in this review, one could also replenish sodium workout losses with either a nutrition supplement or by sprinkling extra salt on food based on the amount of sweat/sodium lost during the training session (Clark, 2014).

**Sample 1-day plan for old age and/or chronic disease prevention (about 2,000 kcal)**

The 1-day menu shown in Figure 35 provides about 2,000 kcal in the form of carbohydrates (55% total kcal), protein (18% total kcal) and fat (27% total kcal). It also provides 1,581mg of sodium, 5.5 % fat kcal from SFA, 175mg of cholesterol and 31g of fiber. In this example, San Daniele ham is offered as part of a healthy lunch. Considering that nutrition recommendations meant to prevent chronic disease encourage to consume less than 2,300 mg sodium, less than 7-10% saturated fat (using kcal from total fat as 100%) and less than 300 mg of cholesterol, this 1-day Mediterranean menu would benefit individuals with old age affected by low stage hypertension and/or wishing to prevent chronic disease.
<table>
<thead>
<tr>
<th>Meal</th>
<th>Food/ingredient</th>
<th>Amount (g/ml or other units)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breakfast</strong></td>
<td>Yogurt, low fat (fruit flavor)</td>
<td>125g (4.4 oz)</td>
</tr>
<tr>
<td></td>
<td>Banana</td>
<td>150g (1 medium fruit)</td>
</tr>
<tr>
<td></td>
<td>Oats</td>
<td>40g (1.4 oz)</td>
</tr>
<tr>
<td></td>
<td>Espresso coffee</td>
<td>40ml (1.4 fl.oz)</td>
</tr>
<tr>
<td><strong>Morning snack</strong></td>
<td><strong>Apple</strong></td>
<td>150g (1 medium fruit)</td>
</tr>
<tr>
<td><strong>Lunch</strong></td>
<td>Farro</td>
<td>50g (1.8 oz) (dry)</td>
</tr>
<tr>
<td></td>
<td>Aragula</td>
<td>100 g (3.5 oz)</td>
</tr>
<tr>
<td></td>
<td>Tomatoes</td>
<td>200 g (7 oz)</td>
</tr>
<tr>
<td></td>
<td>Garlic</td>
<td>2 g (1/2 teaspoon)</td>
</tr>
<tr>
<td></td>
<td>Mint</td>
<td>2 g (1/2 teaspoon)</td>
</tr>
<tr>
<td></td>
<td>Basil</td>
<td>10 g (1 tablespoon)</td>
</tr>
<tr>
<td></td>
<td>Extra virgin olive oil</td>
<td>10 g (1 tablespoon)</td>
</tr>
<tr>
<td></td>
<td>San Daniele ham</td>
<td>50 g (1.8 oz)</td>
</tr>
<tr>
<td></td>
<td>No-salt bread</td>
<td>70 g (2.5 oz)</td>
</tr>
<tr>
<td><strong>Afternoon snack</strong></td>
<td><strong>Yogurt, low fat (fruit flavor)</strong></td>
<td>125 g (4.4 oz)</td>
</tr>
<tr>
<td></td>
<td>Strawberries</td>
<td>50 g (1.8 oz)</td>
</tr>
<tr>
<td><strong>Dinner</strong></td>
<td>Whole grain pasta</td>
<td>80 g (2.8 oz) (dry)</td>
</tr>
<tr>
<td></td>
<td>Zucchini</td>
<td>100 g (3.5 oz)</td>
</tr>
<tr>
<td></td>
<td>Butternut squash</td>
<td>100 g (3.5 oz)</td>
</tr>
<tr>
<td></td>
<td>Mackerel fillets</td>
<td>130 g (4.6 oz)</td>
</tr>
<tr>
<td></td>
<td>Spinach</td>
<td>150 g (5.3 oz)</td>
</tr>
<tr>
<td></td>
<td>Extra virgin olive oil</td>
<td>15 g (1.5 tablespoons)</td>
</tr>
<tr>
<td></td>
<td>Parsley</td>
<td>10 g (1 tablespoon)</td>
</tr>
<tr>
<td></td>
<td>Garlic</td>
<td>2 g (1/2 teaspoon)</td>
</tr>
</tbody>
</table>

Figure 35: Sample 1-day plan for old age and/or chronic disease prevention (about 2000 kcal) (INRAN, 2000; IEO, 2008)

7. FINAL CONSIDERATIONS

Processed meat is a heterogeneous food category, which has raised the question of whether all of its components have the same carcinogenic effects. While more research is needed in this area, this review analyzed dry-cured ham production, composition and health implications, using San Daniele ham as a high quality representative of processed meats. Available research has shown that dry-cured ham is nutritious and research meant to obtain dry-cured ham of even higher quality and nutritional value is promising. On the other hand, to facilitate this process, it is important to address research limitations as well as consumer perceptions about processed meats.

7.1 Limitations of research on dry-cured ham

Discussing dry-cured ham quality is difficult as there are several quality determinants. What is more, research meant to address dry-cured ham quality is influenced by the intrinsic limitations of *in vitro*, *in vivo* and human studies and the fact little information about consumer expectations about quality is available.
Intrinsic limitations of *in vitro, in vivo and human* studies

- **In vitro** studies on curing-related proteolysis frequently fail to account for the GI environment found in living organisms. Only when GI digestion is simulated *in vitro*, it is possible to study the bio-accessibility and availability of bioactive peptides. The latter must resist GI protease degradation and enter the bloodstream via the intestinal epithelium to exert their physiological effects (Gallego et al, 2017).

- **In vivo** studies conducted in living animals such as rats help establish how diet affects health and disease. However, human physiology differs from animal physiology in many respects (Willet et al, 1998). In addition, many farms do not allow researchers due to hygienic restrictions. As a consequence, sample sizes in animal health studies focusing on pigs are frequently low, thus affecting the generalizability of observational data.

- **Human** studies do not necessarily represent real life situations either. Dietary factors such as bioactive peptides or sodium are hardly ever consumed in isolation by humans. On the other hand, studying whole foods or entire food categories prevents researchers from isolating the effects of single nutrients and/or single foods, respectively. What is more, not only chronic diseases are multifactorial and have a long latency period in humans, but also single biomarker changes do not necessarily reflect any changes in disease risk. For example, glucose levels alone may not precisely account for someone’s overall risk to develop diabetes. In addition, although randomized control trials are supposed to provide the best level of evidence, they are expensive and assessing habitual dietary intakes of free-living individuals is complex. Thus, health-conscious volunteers may not represent the general population and, contrary to experiments meant to compare new drugs to placebo, researchers administering whole foods can’t effectively blind participants to the diet of interest (Willet et al, 1998).

Limitations regarding dry-cured ham industry’s ability to identify and meet consumer demands

The relationship between consumer perception of meat quality and/or healthfulness and industry’s ability to meet consumer demands is complex and partially explained by the Total Food Quality Model (TFQM), a frame of reference drawing mainly on European studies regarding beef and pork (Figure 36). According to the TFQM, consumers form expectations about meat quality based on their own experience and the informational cues available in their environment (Grunert et al 2004). Before purchase, quality expectations are based on both intrinsic cues like product’s colour and degree of visual fat, and extrinsic cues such as brand name and price (Troy et al, 2010). After purchase, consumers can verify whether actual quality deviates from expected quality (Grunert et al 2004).

Unfortunately, extrinsic cues such as sensational news about food and diet tend to shed in bad light a variety of food products. For example, the internet offers a variety of opinions about food products, giving consumers the impression that experts always change their mind about what is good and what is bad food wise (Rangel et al. 2012). The consequences of this phenomenon are overall disorientation and the self-prescription of unjustified dietary restrictions (Macdiarmid et al, 2016). Last but not least, although a lot of Italian consumers eat dry-cured ham as part of other foods such as traditional filled pasta (e.g. Tortellini), which contribute to 7.5% of the gross income from pork, few studies have assessed any differences between the health effects of dry-cured ham and its byproducts (Jayathilakan et al, 2012).
7.2 Future perspectives of research on dry-cured ham

Some areas of research, such as genomics and peptidomics, are advancing and promising. In addition to that, studying consumer perceptions about dry-cured ham may help the communication between research and ham industry, with the ultimate goal to help consumers meet their expectations and nutrition needs.

Modern sciences as a tool to create dry-cured ham of higher nutritional value

Genomics is an emerging science involving a qualitative approach and a controlled design as it focuses on genetic mutations located on selected DNA sequences and genomics-based family traits. Hence, as opposed to traditional genetic selection, which involves quantitative approaches that are based on the analysis of multiple phenotypes, pedigree-based family traits and environmental factors, there are some emerging genomic techniques that have made statistical analysis less time-consuming, less expensive, less stochastic and more deterministic. Some emerging genomic techniques include Marker Assisted Selection (MAS), Gene Assisted Selection (GAS) and genome-wide associations (GWAS). They are particularly helpful in the identification of genetic variants that can affect fat and/or lean mass deposition.

Similarly, peptidomics is progressively replacing modern proteomics in the study of biopeptide composition, interactions and properties. Proteomics has always been considered as the perfect link between genomics and physiology. It adopts a “bottom-up” approach as proteins are digested to generate peptides of similar length and properties. Peptidomics, instead, is based on a “top-down” approach that starts with unspecific hydrolysis and ends with the generation of peptides that differ in lengths and post-translational modifications. Furthermore, while proteomics-derived peptides are automatically analyzed by a mass spectrometer (MS), peptidomics helps identify as many peptides as possible via the study of the MS spectra of each peptide (Gallego et al, 2016). With that said, peptidomics could help identify the sequence and properties of bioactive peptides in dry-cured ham so that they could be added to a variety of food products, dry-cured ham included in order to enhance flavour, ameliorate emulsion stability, WHC and increase nutritional value. This may be particularly successful in the Mediterranean area, where trimmings generated from dry-cured ham boning and slicing could be chopped, comminuted and pre-blended to prepare traditional fillings for pasta with higher nutritional value (Mora et al, 2014).
Strategies to improve consumer perceptions about dry-cured ham

Studying consumer perceptions regarding dry-cured ham can help understand how the general public values dry-cured meat. Once consumer beliefs or expectations are identified, it will be easier to provide them with the information they need to make food choices based on their unique needs.

A recent focus group conducted in Northeastern Italy showed that consumers think that food is safe when “it is fresh and in season”, “its quality can be directly or indirectly controlled by the consumer”, “it is not overly manipulated”, “its preparation is associated with a high level of hygiene” and “it comes from personal animal breeding”. However, self-produced food frequently poses a greater microbiological risk than industrial food. Therefore, to prevent common misconceptions, meat producers should develop communication messages to persuade consumers to purchase dry-cured ham from trustworthy vendors and learn the positive health effects of implementing food safety practices at home (Tiozzo et al, 2017).

To further invest in targeted marketing strategies, meat producers could investigate what attributes are appropriate in different countries for communicating the eating quality of dry-cured ham. A recent study involved 3 samples of 30 respondents in Italy, Norway and Spain. Participants were asked to profile six samples of dry-cured ham: two Italian (15-month and 24-month Parma hams), two Spanish (9-month and 18-month Serrano hams) and two Norwegian (4-month and 15-month hams). The consumers from both Italy and Spain, claimed that Norwegian short-aged ham had a smoked odour/flavour and described its texture as fibrous, rubbery, firm, dry, hard and plastic. The same consumers agreed that Italian and Spanish ham had a more intense odor. Although Italian and Spanish consumers shared some vocabulary, possibly because dry-cured ham is a traditional product in Italy and Spain, there were some differences too. To describe Italian hams, Italian consumers mentioned sweetness, ham flavor, raw meat flavor while Spanish consumers did not address any of these parameters. To describe Spanish hams, instead, Italian consumers analyzed rancidity, marbling and moldiness while Spanish consumers focused on flavour intensity (Hersleth et al, 2013). Although this study did not establish whether responses were affected by gender, age or personal beliefs, it helped identify the most common attributes to describe ham: “red color”, “marbling”, “ripe/cured flavor or odor”, “saltiness”, “sweetness”, “firmness” and “tenderness”. These data represent a starting point for meat professionals who wish to meet country-based expectations on dry-cured ham.

7.3 Conclusive remarks

Healthy eating is a consumer’s responsibility. Knowing what we eat, and keeping to a varied, balanced and moderate diet is the first step towards healthy living and aging. Until more research is done to evaluate whether processed meats can have different effects on carcinogenesis and overall health, meat industry is encouraged to partner with food scientists to manufacture healthier versions of dry-cured ham with a correct balance between nutrient composition and sensorial profile. In addition to that, meat industry should partner with nutrition professionals. They can help individual consumers contextualize and clarify the oversimplified statements about processed meat and health that are frequently shared by modern media.

8. ACKNOWLEDGEMENTS

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9. REFERENCES

References grouped by type of resource

Books

Online resources or databases
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References grouped by country*
* whenever authors come from different countries, the last author determines the country variable. For a complete list of references, please refer to the list of references above.

Part I: Introduction
(definitions of healthy eating and lifestyle, processed meats and dry-cured ham) (tot= 22 references)
• Italy (23%): Dernini et al, 2015; IMH, 2012; INRAN, 2003; SINU, 2014; URSANU, 2015
• Spain (14%): Jiménez-Colmenero et al, 2010; Mora et al, 2016a; Toldrà et al, 2007
• Other European Countries (4%): Ivanovic et al, 2016
• USA (23%): Micha et al, 2012; ODPHP, 2015; Turner et al, 2017; USDA, 2012; USDA, 2018
• Asian Countries (0%)
• Other countries (0%)
Part II: Determinants of dry-cured ham quality

a) Pre-slaughter variables (42 references)

- **Spain (18%)**: Avuso et al, 2015; Cisneros et al, 1996; Diaz et al, 2006; Guardia et al, 2004; Guardia et al, 2005; Jiménez-Colmenero et al, 2010; Yang et al, 2011
- **Other European Countries (20%)**: Benjamin et al, 2009; Candek-Potokar et al, 2012; Lebret, 2008; Maw et al, 2001; Meunier-Salau et al, 2006; O'Neil et al, 2003; Piontkowski et al, 2016; Sionek et al, 2016; Terlouw et al, 2005
- **Asian countries (8%)**: Cho et al, 2011; Kim et al, 2006; Zhang et al, 2007
- **Other countries (South America, Canada) (8%)**: Farez et al, 1997; Raymond et al, 2017; Schnoeller et al, 2006
- **International Organizations / Institutional collaborative research (5%)**: Ensembl, 2017; FAO, 2011

b) Post-slaughter variables (47 references)

- **Italy (21%)**: Assica, 2013; Benedini et al, 2012; Gaspardo et al, 2008; Laureati et al, 2014; Merialdi et al, 2016; Paolella et al, 2015; Pareli et al, 2017; San Daniele ham consortium, 2014; Schivazappa et al, 2012; Stefanon et al, 2012;
- **Spain (23%)**: Bayarri et al, 2010; Escudero et al, 2012; Escudero et al, 2013; Gou et al, 1996; Herrero et al, 2017; Martínez-Sánchez et al, 2016; Mora et al, 2016a; Mora et al, 2016b; Ruiz Ramirez et al, 2006; Toldrà et al, 2006; Ventanas et al, 2005
- **Other European countries (21%)**: Candek-Potokar et al, 2012; Coutron-Gambotti et al, 1999; Foury et al, 2011; Gilles et al, 2009; Lebret, 2008; Pichner et al, 2006; Rama et al, 2013; Safa et al, 2017; Sionek et al, 2016; Van de Perre et al, 2010
- **USA (8%)**: AMSA, 2015; Bedale et al, 2016; Scalese et al, 2016; Springer et al, 2003;
- **Asian countries (6%)**: Wakamatsu et al, 2010; Xing et al, 2015; Zhi-Zhou et al, 2015
- **Other countries (Africa, Australia, Canada) (11%)**: Channon et al, 2002; Channon et al, 2014; Paschos A et al, 2013; Ren et al, 2008; Shalaby et al, 2013
- **International organizations / Institutional collaborative research (10%)**: CDC, 2017; EC, 2005; FAO, 2005; Toldrà et al, 2014
Part III: Dry-cured ham and health
a) Nutrient composition and consumption in physiological conditions (27 references)
   • **Italy (26%)**: ASSICA, 2013; INRAN, 2000; IZSV, 2017; Gatorade Italia; SINU, 2014; PDHU, 2018; USDHHS, 2018
   • **Spain (15%)**: Herrero et al., 2017; Jiménez-Colmenero et al., 2010; Martinez Sanchez et al., 2017; Marusic, 2013
   • **Other European countries (29%)**: Biesalski, 2005; Blomstrand, 2006; Dodds et al., 2015; Foure, 2017; Ivanovic, 2016; Jeukendrup, 2011; Witham, 2008; Young et al., 2013
   • **USA (26%)**: ACEND, 2016; ACSM, 2007; Clark, 2014; CDC, 2017; Gropper et al., 2007; GSSI, 2018; You et al., 2015
   • **Asian countries (0%)**
   • **Other countries (0%)**
   • **International organizations / Institutional collaborative research (4%)**: IEO, 2008
b) Consumption in disease settings (25 references)

- **Italy (12%)**: MIPAAF, 2007; Perna et al, 2017; Savanelli et al, 2017
- **Other European countries (16%)**: Biesalski, 2005; Chambers et al, 2015; Ivanovic et al, 2016; Steinert et al, 2011; Young et al, 2013
- **USA (8%)**: Stettler et al, 2013; USDA, 2015
- **Asian countries (12%)**: Fu et al, 2013; Zhang et al, 2010; Zhu et al, 2015
- **Canada (4%)**: Savoia et al, 2007
- **International organizations / Institutional collaborative research (20%)**: Anderson, 2014; Mulvihl, 2004; Toldrà et al, 2014; WHO, 2009b

Part IV: San Daniele and healthy menus (7 references)

- **Italy (71%)**: Gaspardo et al, 2008; INRAN, 2000; MIPAAF, 2007; San Daniele Ham consortium, 2014; URSANU, 2015
- **International organizations / Institutional collaborative research (29%)**: IEO, 2008; Toldrà, 2014
Part V: Conclusive remarks (10 references)

- **Italy (20%)**: Hersleth et al, 2013; Tiozzo et al, 2017
- **Spain (30%)**: Gallego et al, 2017; Mora et al, 2014; Toldrà et al, 2007
- **Other European countries (20%)**: Grunert et al, 2004; Macdiarmid et al, 2016
- **USA (0%)**
- **Asia (10%)**: Jayathilakan et al, 2012
- **Canada (10%)**: Rangel et al, 2012
- **International organizations / Institutional collaborative research (10%)**: Willet et al, 1998

References by country

- Italy
- Spain
- Other European countries
- Asian countries
- Canada
- International organizations / Institutional collaborative research