Review

Proteomics in Argentina - limitations and future perspectives: A special emphasis on meat proteomics

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Argentina is one of the most relevant countries in Latin America, playing a major role in regional economics, culture and science. Over the last 80 years, Argentinean history has been characterized by several upward and downward phases that had major consequences on the development of science in the country and most recently on proteomics. In this article, we characterize the evolution of Proteomics sciences in Argentina over the last decade and a half. We describe the proteomics publication output of the country in the framework of the regional and international contexts, demonstrating that Argentina is solidly anchored in a regional context, showing results similar to other emergent and Latin American countries, albeit still far from the European, American or Australian realities. We also provide a case-study on the importance of Proteomics to a specific sector in the area of food science: the use of bacteria of technological interest, highlighting major achievements obtained by Argentinean proteomics scientists. Finally, we provide a general picture of the endeavors being undertaken by Argentinean Proteomics scientists and their international collaborators to promote the Proteomics-based research with the new generation of scientists and PhD students in both Argentina and other countries in the Southern cone.

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1 Introduction

The Argentine Republic, known usually simply as Argentina, is the country with the second highest land area in South America, ranking eighth in the world. Argentina has a population of over 42 million, of which an estimated 25% live in the metropolitan area of the major and capital city, Buenos Aires. Argentina is considered a middle or regional power with strong economic sectors, particularly in Agriculture and Livestock production. Argentina declared independence from Spain in the early 19th century and, up until the late 1940s has historically attracted massive numbers of European emigrants, particularly from Spain, Italy, Germany, Portugal and neighboring countries. The massive arrival of emigrants, the high-amount of mineral, agricultural and fisheries resources, together with an early industrialization, particularly around the Buenos Aires and the Rio de la Plata area, have contributed to a steady growth of the economy that historically has relied on the export of raw products such as beef, fish, fruits or wheat, but also processed agricultural products like fruit concentrates or sugar. The growth of the economy that in the 1930's was amongst the highest in the World, was followed by strong successes in the educational and scientific fields, quite unique in the Latin America context [1]. However, during the last 50 years, Argentina has experienced particular historical

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circumstances not very favorable to the development of science that culminated in the emigration of Argentinean scientists and skilled professionals [2]. In the last decade however, the country has struggled to curb these problems. Argentina is considered a country with a high Human Development Index ranking 45th place, with a 0.797 score, very similar to countries like Chile (0.805), Portugal (0.809) or Poland (0.813) [3].

The first institutions of scientific research in Argentina, emerged in the early 20th century and had their location at public (National) universities such as Córdoba, Buenos Aires and La Plata. Scientific research reached its moment of greatest visibility and maturity, in accordance with international trends, during the 1950s and 1960s (although the Physiology/Medicine Nobel prize had been awarded to Bernardo Houssay already in 1947) [4]. The most important institutions to design and implement policies aimed at scientific and technological development in Argentina were established in the second half of the fifties. The National Atomic Energy Commission (CNEA) was created in 1950; the National Institute of Industrial Technology (INTI) was created in 1956; the National Institute of Agricultural Technology (INTA), in 1957 and the National Council of Scientific and Technical Research (CONICET), in 1958. The latter institution first Director was in fact Bernardo Houssay, and CONICET was conceived as an instrument to promote scientific research in universities and was partly inspired by the model of the French CNRS (Centre National de la Recherche Scientifique). Finally from 1996 onwards a novel structuring strategy was undertaken by the institutional system by redefining the goals and roles of research organisms. In particular, public R&D was emphasized and oriented towards the innovation needs of the productive sector. For this purpose the National Agency for Scientific and Technological Promotion (ANPCyT) with its two funds: the FONCYT, to fund research projects, and FONTAR to promote innovation and modernization of the productive sector was also created.

The period comprising the early sixties and the turn of the century has witnessed a significant economic and scientific stagnation in Argentina caused by several crisis of political and social nature that led to a relevant scientist migration. In half a century scientists such as the Nobel Prize winner César Milstein (1984), were exiled abroad, never to return. In total, it is estimated that 4000 Argentine scientists left the country during the 1966–2002 period in a veritable "brain-drain". In the 1990s, as the country began to confront its recent history, economics constraints kept on. During the Argentinian financial crisis that peaked in 2002, with the default crisis and the local currency (Argentinean peso) devaluation a new generation of scientists left the country.

The panorama began improving in recent years — and a 'brain gain' has been credited to the government. In 2007, the country's first science ministry was established and Science was on the political agenda with several programs created, not just for funding, but also in the form of fellowships and positions for scientists in Argentina to reverse the brain drain and to retain scientists. In fact, in 2008 and more recently in 2014 the journal Nature devoted several optimistic comments/news about the statement of the new Ministry of Science and praised government's science policies in Argentina [5–7]. Since 2008, over 1130 Argentine scientists have returned through the RAICES (Spanish for Roots) program. This was designed to encourage researchers to return home with offers of equipped laboratories and salaries comparable to those in the United States and Europe. Moreover 500 researchers and 1500 trainees were then hired annually, with an expenditure of over ARS$ 450 million (49 million US$) for scientific and technological institutions in the country, leading to established high-capacities in biomedicine, nanotechnology and nuclear energy. Among the most relevant achievements in 2013 are the launch of the Argentina Innovadora 2020, the National Plan of Science, Technology and Innovation; the hiring of 1907 new PhD and post-doc fellows within the Internal Scholarship Program CONICET, reaching a total of 8877 trainees.

Nevertheless, by the end of July 2014, Argentina defaulted on international debt payments for the second time in 13 years. So far, the situation has been relatively mild compared with the recession that followed the December 2001 default. Yet concerns have been raised about its long-term effects. However, it is still not clear how the default will impact researchers. A significant risk for science is the loss in purchase power with the Argentinean peso devaluation. In the last ten years an increase in grants and in funds available to buy equipment for laboratories has been recorded. However, devaluation of the national currency will lead to higher relative costs of scientific equipment and reagents hampering laboratory re-equipment with subsequent difficulties in competitiveness. To tackle the problem, the ministry of science and technology put forward mechanisms to speed up the import procedures but import procedures are still difficult and are taking longer than before [8].

An important strategy to circumvent economic constraints is to strengthen ties to foreign researchers that can help to improve the scientific enterprise in Argentina as well as in South America. In fact, from London to Boston and Tokyo, individual scientists and larger organizations can offer significant help to South American countries mainly by hosting young scientists in laboratories. Although there is a clear need for scientists from Europe and North America to visit Argentina and Latin America as well (for details kindly refer to the articles in the special number of Nature 2014, available at: http://www.nature.com/news/specials/southamerica-1.15370).

Animal and food of animal origin research in Argentina covers a large number of topics areas from animal diseases/welfare to control of livestock production systems of animals with economic importance such as swine, beef and small ruminants, as well as non-traditional animals namely llama or chinchilla [9–13]. In the last 15 years, about 522 publications were retrieved when "farm, animal and Argentina" were used as key words in bibliography search engines such as Scopus or Biblioteca Electrónica de Ciencia y Técnica de la Argentina. This simple statistics provides a notion on the

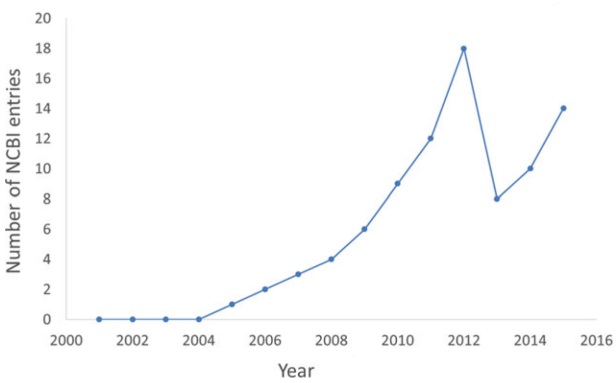

Figure 1. Evolution by year (2001- May 2015) of the hits in Medline with the words Proteomics and Argentina.

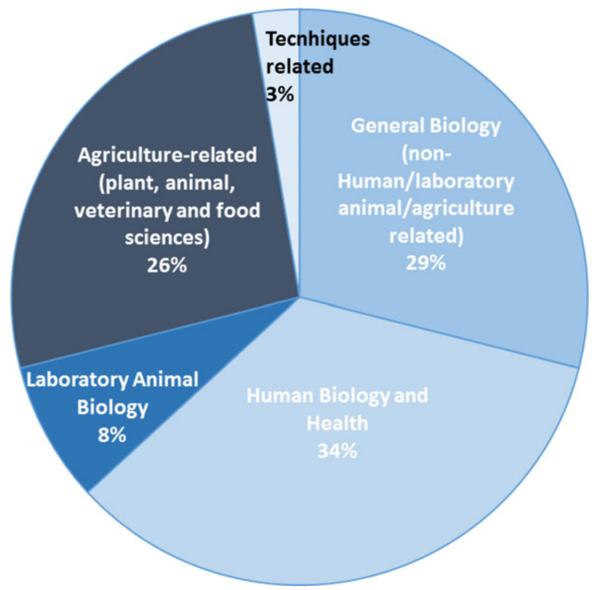

Figure 2. Distribution of Proteomics literature (2001–2015) according to the major areas. Note the importance of agricultural, animal and food sciences, representing over 25% of the total number of papers indicating the importance of the sector in Argentinean research.

importance of the sector and the relevance of research in animal science for the country.

This article aims to provide an overview of the current Argentinean Proteomics Science status. We particularly focused on the use and potential of proteomics in farm animal research as seen in other parts of the world, namely Europe [14] or the United States of America [15,16]. In a first section, we will focus on the current status of Proteomics research in Argentina in a transversal approach across different research areas. We will draw a comparison with other major countries in Latin America, with emerging countries as well as with countries in Europe, North America and Australia. Subsequently, we will address the major constraints to Proteomics research in Argentina. On a second section, we will characterize the current status of animal and veterinary proteomics research in Argentina by providing study case examples. On a third section, we will address efforts conducted to the dissemination and training of Argentinean life scientists in proteomics and mass spectrometry, presenting recent case studies and examples of proteomics training in the country. In a final section, we will present our overview on the potential for Proteomics in Farm Animal research in Argentina and how such potential could be untapped and further developed.

2 Proteomics research in Argentina an overview

Within the previously described scenario, and given that Proteomics based research requires stable funding and access to state of the art, expensive mass spectrometers, it could be said that Proteomics research in Argentina is still very limited. In fact, and if we conduct a search for the 2001–2014 period in the Pubmed (http://www.ncbi.nlm.nih.gov/pubmed) database with the words Argentina and Proteomics, only 69 articles would be retrieved (with an additional 14 until the 1st May 2015). If we distribute that number by the period, as plotted in Fig. 1, it is clear that Argentina only entered the world of Proteomics literature in the year 2005 when one paper on Proteomics was published.

Nevertheless, and interestingly, as fruit of the abovementioned conditions, this number had a continuous growth until the year 2012 when a total of 18 Proteomics/Argentina papers were retrieved in Pubmed. During the last 2 years the number of entries seems to have declined to about half those recorded for the 2012 peak. Such evolution could likely be attributed to the 2008 world financial crisis that led to cuts in science funding throughout the world, and particularly in countries already hit by several economic problems such as those recently afflicting Argentina. However, this tendency seems to change because so far in 2015 have already been published 14 Proteomics/Argentina articles which indicate a renewal of Proteomics research in Argentina. We have subsequently divided the papers published by five major areas within proteomics research: (i) General Biology (non-Human/laboratory Animal or Agriculture related); (ii) Human Biology and Health; (iii) Laboratory Animal Biology related; (iv) Agriculture-related (plant, animal, veterinary and food sciences) and (v) Techniques related proteomics. Results are described in Fig. 2. As expected, human biology and health as well as laboratory animal related proteomics comprise a significant amount of the publications (respectively 35 and 8%), whereas general biology accounts for 29% of the publications. Interestingly, and as a clear representation of the agricultural and animal production sectors in Argentina, domestic plant and farm animal proteomics accounts for a very significant proportion of the publications, with over 25% of the publications. Finally, and as expected, proteomics techniques development related papers are virtually inexistent as evidenced by the number of publications in this area (3%). This data clearly places Argentina as an end-user of applied standard proteomics techniques.

When looking at the number of papers published, it is noteworthy to mention that if a similar search would be conducted for the major countries in Latin America (Brazil, Mexico, Argentina, Chile, Colombia, Peru and Venezuela) as plotted in Fig. 3a and b, it is clear that Argentina would rank as number 3 in number of Proteomics entries in NCBI, with the two upper places led by Brazil and Mexico (Fig. 3a). If the number of publications retrieved is divided by the number of population of the country (per million inhabitants), it is clear that Latin America Proteomics is dominated by Brazil and Chile, with Argentina and Mexico respectively in the 3rd and 4th places (Fig. 3b). As such, it could be said that the Argentinean Proteomics scenario is well inserted in the Latin American context. The same could be said for a comparison with the so called "emerging nations". In our case we have chosen, in addition to Argentina, Mexico, Brazil, People's Republic (P.R.) of China, Russia, Turkey, South Africa and India. Results are depicted in Fig. 3c and d. As shown, P.R. China, India and to a less extent Brazil are the main countries regarding the number of Proteomics NCBI entries. Nevertheless and as results are shown per million inhabitants, it could be said that the three Latin American nations are second only to P.R. China in number of Proteomics entries per million inhabitants, with the rest of the emerging countries (Russia, Turkey, S. Africa and India) showing less entries per million inhabitants than Argentina. Finally, and as shown in Fig. 3e and f, the results obtained by Argentina regarding the absolute number of Proteomics entries in NCBI and the Number of entries per million inhabitants is still much lower that the values recorded for Japan, Australia, the United States of America as well as most of the European countries, regardless of their size and research environment.

The analysis of the previously described data seem to indicate that Proteomics research output, as it could be retrieved from NCBI, falls within Latin American and Emerging Countries realities, nevertheless far from results obtained in countries in Europe, North America and Australia. There seems therefore that Argentina clearly faces a considerable number of pitfalls, mostly related to peculiar economics and funding constraints shared by several countries. It would also be worth mentioning that a survey such as the one herein mentioned reflects only papers with Argentinean scientists, regardless of the nature of the paper. In fact, pertinent questions such as for instance if the paper is solely Argentinean or in collaboration with other countries, still remain unanswered and could only be completed through a much broader survey and analysis.

The major constraints faced by proteomics in Argentina are common to many other countries in the world, particularly those facing some degree of financial restrictions. This means that funding is without doubt the most important set-back in the development of Proteomics research in Argentina. Naturally, funds are essential and have to be available to support proteomic experiments. In Argentina money availability encounters additional difficulties, in particular the fact that most imports, such as reagents and equipment, have to be justified and approved by the authorities as hard currencies have to be used. This makes the whole process very time consuming, difficult and expensive if we count the time and resources researchers have to allocate to such tasks. The situation implies that all experiments have to be carefully elaborated and scheduled as it is frequent more than six months delay in reagent reception. This means that there is little room for strategy changes or trying new approaches and experimental techniques delaying publications and project outcomes. This is particularly hindering in cutting edge techniques such as Proteomics and other Omics. Another difficulty in Argentina is related to lack of access to national proteomics platforms. Currently and to the best of the knowledge of the authors, there is only one national proteomic platform facility harboring Mass Spectrometry services (the CEQUIBIEM, http://www.qb.fcen.uba.ar/cequibiem/). In a country with the dimension of Argentina this is particularly problematic, as makes access difficult to most researchers outside of the Buenos Aires area and it also renders difficult interaction between researchers and the mass spectrometer operators. As such, the collaboration with foreign platforms is frequently the only solution to overcome this issue. Again and given the distances in Argentina, the lack of access to necessary commodities necessary for shipment (particularly dry ice) can make such collaboration a very difficult task. It is finally worth mentioning that all these problems have contributed to a generalized lack of well equipped labs applying proteomics techniques, from two-dimensional electrophoresis (2DE) to gel analysis and mass spectrometry based protein identification.

It seems therefore that for an increase in Proteomics output in Argentina it is vital to act on five different levels:

(i) increase funding;
(ii) ease the bureaucratic burden on reagent import;
(iii) create conditions for additional MS platforms;
(iv) increase the awareness of scientists on Proteomics techniques and achievements;
(v) increase the training of PhD students, post-docs and staff scientists on Proteomics.

3 Proteomics in animal science research in Argentina: Interesting case studies

Working with farm animals and with food of animal origin, proteomics presents a considerable number of difficulties and challenges, particularly related to the low representation in protein databases [17]. This means that with the exception of pig [18], rabbit [19] and cattle [20], all other species and in many cases, bacteria associated with the manufacture of specific products like cheese and sausages,

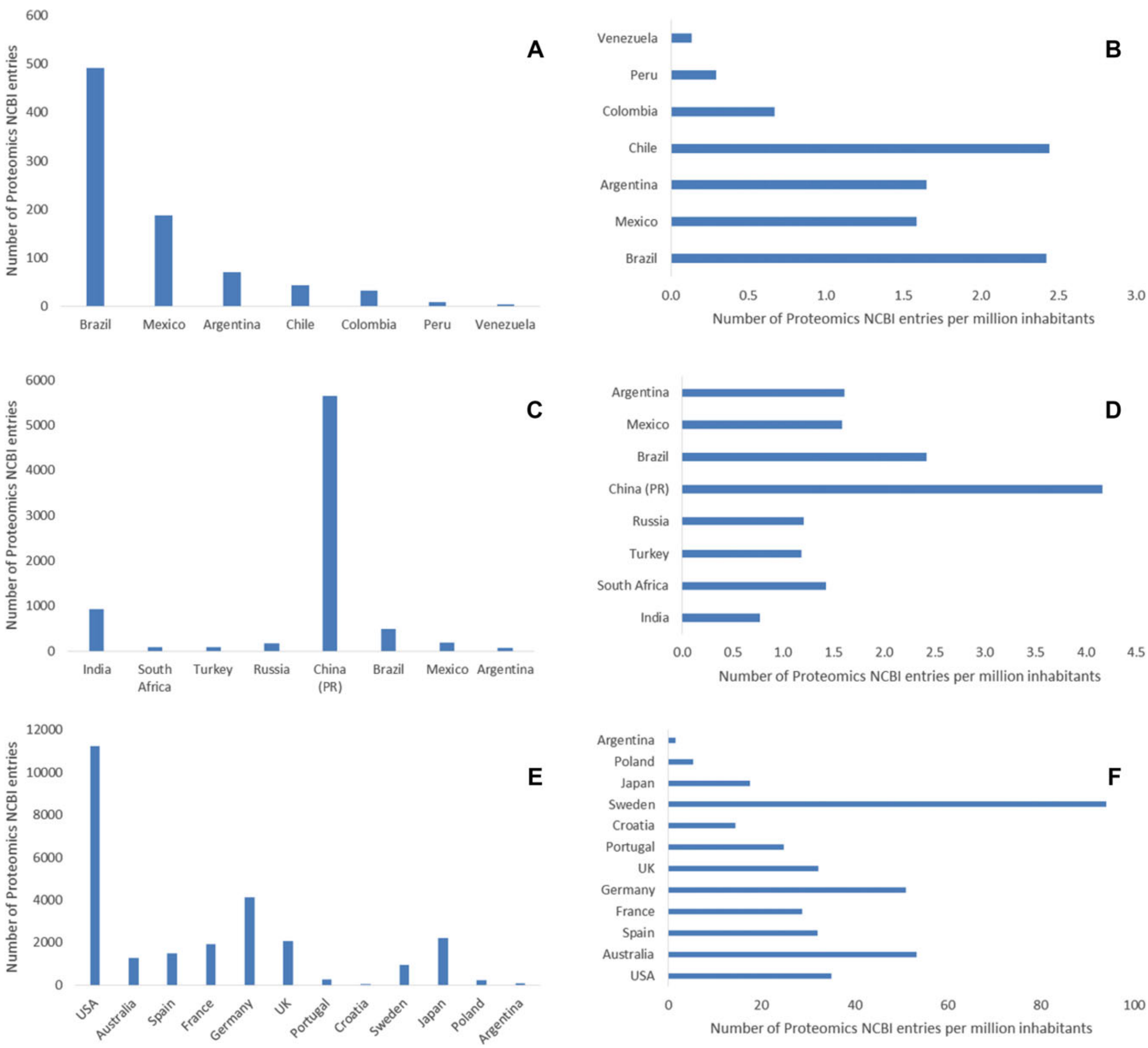

Figure 3. Number of hits in Medline for Proteomics and Argentina and several other Latin America, Emerging and Industrialized countries. (a, c and e) – Absolute number of hits; (b, d and f) – Number of hits per million inhabitants. Latin America: Brazil, Mexico, Argentina, Chile, Colombia, Peru and Venezuela. Industrialized countries: USA, Australia, Spain, France, Germany, UK, Portugal, Croatia, Sweden, Japan, Poland and Argentina. Emerging countries: Argentina, Mexico, Brazil, China, Russia, Turkey, South Africa and India.

can prove to be difficult to study using proteomics. Nevertheless, Proteomics applications are numerous ranging from meat to dairy sciences [21, 22] and have been considered a strategic new tool for animal science [23]. For further reading we recommend the recent review by Almeida et al., (2015) [14]. It could therefore be inferred that the potential for applying proteomics in a country where animal production has such a strategic relevance would be a reality. However, and as seen in the previous section, proteomics in Argentina still needs to be further developed. In this section we will show different case studies with examples on how proteomics was used in Argentina, and more specifically, in the Reference Center for lactobacilli (CERELA), to study specific aspects within this field, in particular the use of Lactic Acid Bacteria of technological interest in food science.

Lactic Acid Bacteria are the preferred bacteria as bioprotector agents or for starter culture formulation for meat and other raw materials (milk, vegetables and cereals). Ideally, the appropriate cultures have to be selected, in order to be more competitive, well-adapted to a particular product, and with high metabolic capacities to beneficially affect quality and safety of the product and preserve their typicity [24]. The rapid expansion of proteomics built upon the available bacterial genome sequences has provided new approaches for bacterial functional genomics. In combination with transcriptional profiling, proteomics provides access to interesting candidate genes and proteins that can be further characterized by physiological, biochemical and genetic traditional analyses. The action of multiple gene sets can be now revealed by the combined technologies of genomics, proteomics and bioinformatics. In consequence, proteomics opens new perspectives for bacterial biopreservation or starter research purposes [25, 26]. As other bacteria, LAB are affected by harsh environment conditions during food processing. The knowledge of the mechanisms involved in such adaptations is thus essential for selecting the most efficient strains for a particular product. Variations in temperature, osmotic conditions, oxidative or acidic environments are situations to which LAB are routinely subjected. Currently, the proteomic approach constitutes a valuable tool for understanding those adaptive mechanisms [26]. To unravel metabolic strategies of *Lactobacillus (Lb.) sakei* 23K for the adaptation to meat environment, the presence of sarcoplasmic and myofibrillar proteins in the Chemically Defined Medium during bacterial growth were evaluated by a physiologic and proteomic approaches [27]. Results showed that each type of meat proteins produced a different effect on *Lb. sakei* protein expression: myofibrillar proteins exclusively regulated the expression of *Lb. sakei* 23K proteins related to energy, lipid and amino sugar metabolisms, cofactor/ vitamin biosynthesis and cell wall formation, while cellular processing and signaling proteins were modulated only by sarcoplasmic extracts. Notably bacterial proteins related to stress were found to be synthesized in lower amounts in presence of both, sarcoplasmic and myofibrillar proteins. Thus meat proteins would not represent a stress environment *per se* for *Lb. sakei* 23K, in contrast to the other harsh conditions during meat processing (cold, salt, redox potential variations) [27].

On the other hand bacterial cells have developed strategies for their acclimation to osmotic stress such as the intracellular accumulation of compatible solutes (glycine-betaine, proline, trehalose and glycerol), which equilibrate cellular osmotic pressure [28]. Belfiore and co-authors [29] studied the adaption of the anchovy isolate *Lb. sakei C*RL1756 to salted environments in the presence of osmoprotectants. Glycine-betaine (GB) pre-treated cells exposed to 10% NaCl showed improved adaption, achieving growth after a long lag phase while cell growth was not observed in the salted medium without GB. Proteomic analyses revealed decreased synthesis of some glycolytic enzymes and induction of some other. The malate dehydrogenase (MleS) and pyruvate oxidase (Pox2), related to an alternative energetic pathway, were induced to counteract the decreased synthesis of glycolytic enzymes under hypertonic stress for cellular metabolism maintenance. Proteins belonging to general stress response and nucleotide metabolism were up-regulated. Noticeably, the induction of DyP-type peroxidase, involved in iron transport, detoxification and oxidative stress, was observed in this strain under osmotic constraint. The addition of GB as compatible solute was crucial for *Lb. sakei* CRL1756 to overcome this major osmotic constraint. The natural presence of GB in fish guarantees better adaption of *Lb. sakei* CRL1756 to salted environment ensuring its robustness and stability as starter culture for salted anchovy products [29].

Unlike proteomics, peptidomics has the potential to uncover processing sites of precursor proteins. These peptides should be analyzed in their native forms. In some cases, peptidomics has been advocated to the study of the meat peptides generated by the action of endogenous proteases some of them related to sensory attributes [30, 31]. A peptidomic analysis has been undertaken by López et al. [32] to characterize the proteolytic compounds present in commercial fermented sausages. Results showed that low molecular mass peptides (LMW peptides) (between 1000 and 2100 Da) were arisen from both type of muscle proteins indicating that myofibrillar and sarcoplasmic proteins were affected during fermentation and ripening. Due to the wide variety of cleavage sites deduced from their positions on the parental protein, the involvement of both muscle and bacterial proteolytic system on their production was suggested. Further in vitro studies, using a beaker sausage model, have been carried out to identify fragments of sarcoplasmic meat proteins generated in the presence of a selected starter culture (*Lb. curvatus* CRL705 and *Staphylococcus vitulinus* GV 318) compared to a non-inoculated control. Results obtained from the LC-ESI-MS/MS analyses showed a significant increase of LMW peptides after 10 days of incubation at 22°C in both studied conditions (sterile and inoculated) due to the action of both muscle and bacterial proteolytic system. Although the greatest peptides diversity was obtained by the action of the mixed starter culture. Peptides mainly arose from myoglobin, creatine-kinase, glyceraldehyde-3-phosphate-dehydrogenase and fructose-biphosphate-aldolase A (ALDOA). ALDOA hydrolysis was attributed to the mixed starter culture; the released peptides could act as biomarkers for a specific sausage technology [33].

Another team from CERELA has reported the importance of bioactive peptides from milk proteins by means of a peptidomic approach. Proteinases of lactobacilli have key roles in bacterial nutrition and contribute to the development of the organoleptic properties of fermented milk products. In addition, they can release bioactive health-beneficial peptides from milk proteins. In this work, Mass-spectrometric screening of the main peptide peaks derived from proteinase activity, allowed the identification of 33 and 32 peptides in the α_{S1}- and β-casein hydrolysates, respectively. In this pattern, a series of potentially bioactive peptides (antihypertensive and phosphopeptides) encrypted within the precursor protein could be visualized [34]. In another work, the contribution of *Lactobacillus delbrueckii* subsp. *bulgaricus* CRL 454 on proteolysis of β-Lactoglobulin (BLG), the main whey protein, which is poorly digested and highly allergenic, is studied. Peptides derived from hydrolysis of the allergenic sequences (V41-K60, Y102-R124, C121-L140 and L149-I162) were found and identified by LC–MS/MS mass spectrometry. Interestingly, peptides possessing antioxidant, ACE inhibitory, antimicrobial and immuno-modulating properties were found in BLG degraded by the *Lactobacillus* strain and digestive enzymes. Authors concluded that pre-hydrolysis of BLG by *Lb. delbrueckii* subsp. *bulgaricus* CRL 454 has a positive effect on BLG digestion and could diminish allergenic reactions [35].

In this context, Proteomics demonstrated to be a valuable tool, contributing to the selection of starter cultures able to compete and produce metabolites of technological or health interest. It is expected that the information gained by the proteomic approach will lead to a knowledge-based selection of LAB. In addition, the comprehension of the *in situ* behavior of starter cultures by means of the post genomic technologies will contribute to improve fermentation processes as well as to a better understanding of microbial adaptation strategies for obtaining functional cultures with improved capabilities [26].

As can be seen by the focused case studies described above, food proteomics research is in progress, despite all the difficulties described before. It is worth mentioning that the major part of works were undertaken by Argentinean researchers in collaborative projects with European laboratories, which provides Proteomic and MS platforms for separation and identification of studied proteins/peptides as well as scientific background in this field. In some of the described works, Argentinean researchers carried out experiments at their laboratories and samples send to European MS platforms. Otherwise Argentinean agents developed all the work at their foreign partner laboratory in the frame of cooperation projects such as ECOSud Program (scientific bilateral cooperation between Argentina and France). In addition, proteomics development is being carried out by groups from CERELA as well as from other local and national Research Institutes and Universities by means of ongoing projects. Taken together with the number of publications of first half of 2015 we can assume that a progression in proteomic science by Argentinean researchers will take place in the near future. However human resource formation on the proteomic field is mandatory to achieve the required development of proteomics to position Argentina at US and European level.

4 Scientific collaborations and proteomics training initiatives in Argentina

4.1 International scientific collaborations: An opportunity for proteomics research in Argentina

The international situation means that cooperation will gain increasing importance globally over the next years. That is why, in recent years new approaches for international cooperation have been promoted by the Argentinean State, aiming primarily to allow more and better contributions to achieve development goals.

In this sense, and as mentioned before, international cooperation plays a leading role in the field of Argentine science and technology as well as for new developments with added value, according to the National Plan for Science, Technology and Innovation from the Ministry of Science, Technology and Productive Innovation (MINCYT). Accordingly, CONICET (and MINCYT) is presently engaged in international cooperation with institutions in charge of scientific and technological promotion and with other prestigious academic organizations from more than 30 countries through various co-funded instruments, such as Bilateral programs (involving two countries), scientific visits (for Argentinean researchers), International Associated Laboratories (research institutes with at least two locations, one in Argentina and another in counterpart country, established to deepen and consolidate existing links and fruitful scientific cooperation), International Research Centers (units of shared management with foreign institutions). Such co-management includes government, planning and financing as well as travel and accommodation costs for Foreign Scientists and Experts. As part of the Projects, trips and stays for the Argentinean or foreign researchers are also funded. In addition, in some of those projects, scientific instruments are also financed. For instance, 2015 Bilateral Cooperation Projects calls will be held with the Academy of Sciences of Germany (DFG - Germany), Austrian Science Foundation (FWF - Austria), ECOS-Sud (France), Foundation for Research Support of the State of Sao Paulo (FAPESP) in Brazil, Slovak Sciences Academy (SSA), National Institutes of Health (NIH), National Science Foundation of the United States (NSF), Academy of Sciences of the Czech Republic (CAS) and the National Agency for Research and Innovation (ANII) from Uruguay. Although in recent years other countries such as Portugal (FCT: Fundaçaopara a Ciência e a Tecnologia), Romania (Ministry of Education, Research, Youth and Sports MECTS) or India (Department of Science and Technology DST) have also participated as counterparts in bilateral projects (http://www.conicet.gov.ar/cooperacion-internacional/).

Other instruments of cooperation allowed Argentinean scientist to be involved into important international projects, as for instance the Reciprocal Arrangement Argentina-COST signed, in 2010, between MINCYT, Buenos Aires and the COST office in Brussels. COST is the longest-running European framework supporting trans-national cooperation among researchers, engineers and scholars across Europe and other non-European countries (Argentina, New Zealand, South Africa and until recently Australia). In fact this arrangement established the basis of the reciprocal cooperation in the mutual interest of Argentinean and European scientists for COST actions. In line with the principles of the COST financial rules, Reciprocal Short Term Scientific Missions (RSTSM), under this reciprocal agreement can therefore be promoted. In fact, this article was made possible precisely by one of such RSTSMs that amongst other objectives aimed the development of a stronger Proteomics research capacity

Table 1. Examples of courses on Proteomics in Argentina

Course name	Organizer/city/date	Major subject	Target audience	Link
Basic concepts and tools of functional Proteomics: Theoretical bases and applications	IMBICE, CONICET – CICPBA, La Plata, May 2015	Basic concepts for Proteomics and MaldiTof MS MS; de novo sequencing	Local PhD/post-doc students, scientists	http://posgrado.blog.unq.edu.ar/wp-content/uploads/sites/7/2014/04/Curso-de-Proteomica-2014.pdf
PROTEOMICS: Key tool toward biomarker discovery and evaluation	IBYME-CONICET Buenos Aires, October 2014	Basic proteomics (sample preparation, mass spectrometry, data analysis)	Local PhD/post-doc students, scientists	http://www.ibyme.org.ar/capacitacion/3/cursos/138/proteomica-herramienta-clave-para-la-identificacion-y-evaluacion-de-biomarcadores
Introduction to the global analysis of gene expression through Proteomics	CERELA-UNT, Tucumán, September 2014	Introduction to Proteomics and Systems Biology; analysis of 2D gels, Introduction to MALDI; writing an article with a proteomics approach; Proteomics applications (prokaryotes, plants and animals). Practice: 2DE.	Local PhD/post-doc students, scientists	http://www.fbqf.unt.edu.ar/posgrado/Cursos%20de%20posgrado%202014.pdf
Introduction to Proteomics. Applications in protein identification and characterization	National University of San Luis - RedBio Argentina, San Luis, December 2013	General considerations. Theoretical and practical aspects. Technology applied: (1D and 2D PAGE, 2D-HPLC and MudPIT, LabChip. Proteomics in practice, identification, characterization and protein quantification (relative and/or absolute). Strategies to study markers of different biological samples. Bioinformatics. Data and analysis and results interpretation (practice).	Local PhD/post-doc students, scientists	http://www.redbioargentina.org.ar/News/Arch/8_13CursoProteomicaUNSL_AV.pdf
Global genome in action: Study of methodology and applications	CABBIO-LELOIR-CONICET-UADE, Buenos Aires, October 2011	*Genomics*: theoretical bases; sequencing strategies bioinformatics: Theoretical bases. *Transcriptomics*. *Proteomics*: 2DE and MS. Data bases management; practice: Microarrays.	PhD/post-doc students, scientists from Brazil, Uruguay, Paraguay and Argentina	https://www.facebook.com/notes/universidad-argentina-de-la-empresa-uade-oficial/curso-estudio-global-del-genoma-en-acci%C3%B3n-metodolog%C3%ADa-y-aplicaciones/274339902582645
Introduction to Proteomics: 2DE and protein identification by MS	National University of Mar del Plata (UNMP), Mar del Plata, September 2012.	Basics proteomics (sample preparation, mass spectrometry, data analysis. Post translational modifications. Mass spectrometry. Theoretical and practical	Local PhD/post-doc students, scientists	http://www.mdp.edu.ar/exactas/images/pdf/postgrado/oca1221.12.pdf

Table 1. Continued

Course name	Organizer/city/date	Major subject	Target audience	Link
Genes to proteins introduction to global gene expression analysis	CERELA-UNT-CABBIO, Tucumán, November 2012.	*Genomics*: Theoretical bases; sequencing strategies bioinformatics: theoretical bases. Data bases; data mining. *Transcriptomics*: Lactic acid bacteria studies in gene expression (RNA seq; microarrays; real time PCR. *Proteomics*: 2DE and MS: theoretical and practical applications.	PhD/post-doc students, scientists from Brasil, Uruguay, Colombia, Mozambique and Argentina.	http://web.unillanos.edu.co/docus/Calendario%20Cursos%20CABBIO%202012%281%29.pdf
Introduction to Proteomics	CERELA-UNT, September 2007, Tucumán	Introduction and general principles. 2DE; Sampling; Gel analysis using specific software. Introduction to MS MaldiTof. Bioinformatics; databases management. Application of Proteomics (biomedicine, microbiology, food grade).	Local PhD/post-doc students, scientists	www.cerela.org.ar/docs/cursodeproteomica.doc
Introduction to Proteomics	Instituto de Medicina y Biología Experimental de Cuyo (IMBECU), Mendoza. March 2007	Definitions (ome and omics) and general considerations. Theoretical and practical aspects. Global studies and targeted proteomics	Local PhD/post-doc students, scientists	http://argenbio.org/index.php?action=notas&note=3326

and know-how in Argentina as well as the dissemination of the possibilities and strengths of Proteomics research to Argentinean researchers and PhD students.

4.2 Proteomics training in Argentina

Generally speaking, the vast majority of Argentinean researchers working in the field of proteomics could be considered to have received their training outside of Argentina, particularly in Europe and North America, either by attending specific Proteomics courses or with effective "hands on" type of training. Nevertheless, in recent years, young post-docs and PhD students have been trained in proteomics through the organization of short theoretical or theoretical and practical courses (1–2 weeks maximum length). Instructors for such courses are typically senior scientists from Public Universities and Public Research Institutes (e.g. CONICET, INTA) that work in the field, that having started abroad, now conduct proteomics research in an Argentinean institution. Frequently, researchers from foreign institutions are also invited to participate in these courses, particularly in the framework of CABBIO, the Brazilian-Argentinean Biotechnology School (EABBIO). These courses are typically the first exposure of a future young Argentinean researcher to Proteomics. Eventually, and depending on the needs and nature of the PhD or post-doc projects, with proteomics work, it will all evolve into a veritable Proteomics experience. It is noteworthy to mention that institutions such as Universities, CONICET or CABBIO are important instruments to economically support proteomic courses. In fact, and contrary to Europe or North America, commercial companies with strong interests in Proteomics by providing equipment and material for proteomic studies seldom organize training seminars or courses in this particular field. Hence, CONICET for instance frequently, and via specific funding lines and the Post graduate Secretary from individual Universities, provide most of the economic support.

Such different proteomics courses have been organized, from 2007 to 2014 by CONICET, CABBIO or by different National Universities. Around 12 courses were held in different provinces of Argentina such as Mendoza, Mar del Plata, Tucumán, La Plata, San Luis and Buenos Aires (Table 1).

CERELA-CONICET for instance has organized three post graduate courses with proteomics as main topic subject. The first one "Introduction to proteomics" was held in CERELA-CONICET, S.M. Tucumán, in 2007 with the participation of foreign invited and Argentinean specialists among other local researchers. In 2012 another course supported by CABBIO and Tucuman University was organized in CERELA/CONICET. It was called "From Genes to Proteins: introduction to global analysis of gene expression". In this course genomic and proteomic specialists from Brazil, Spain and Argentina participated as professors. This was a very international course as students from Brazil, Uruguay, Colombia and Mozambique, in addition to Argentinean, also

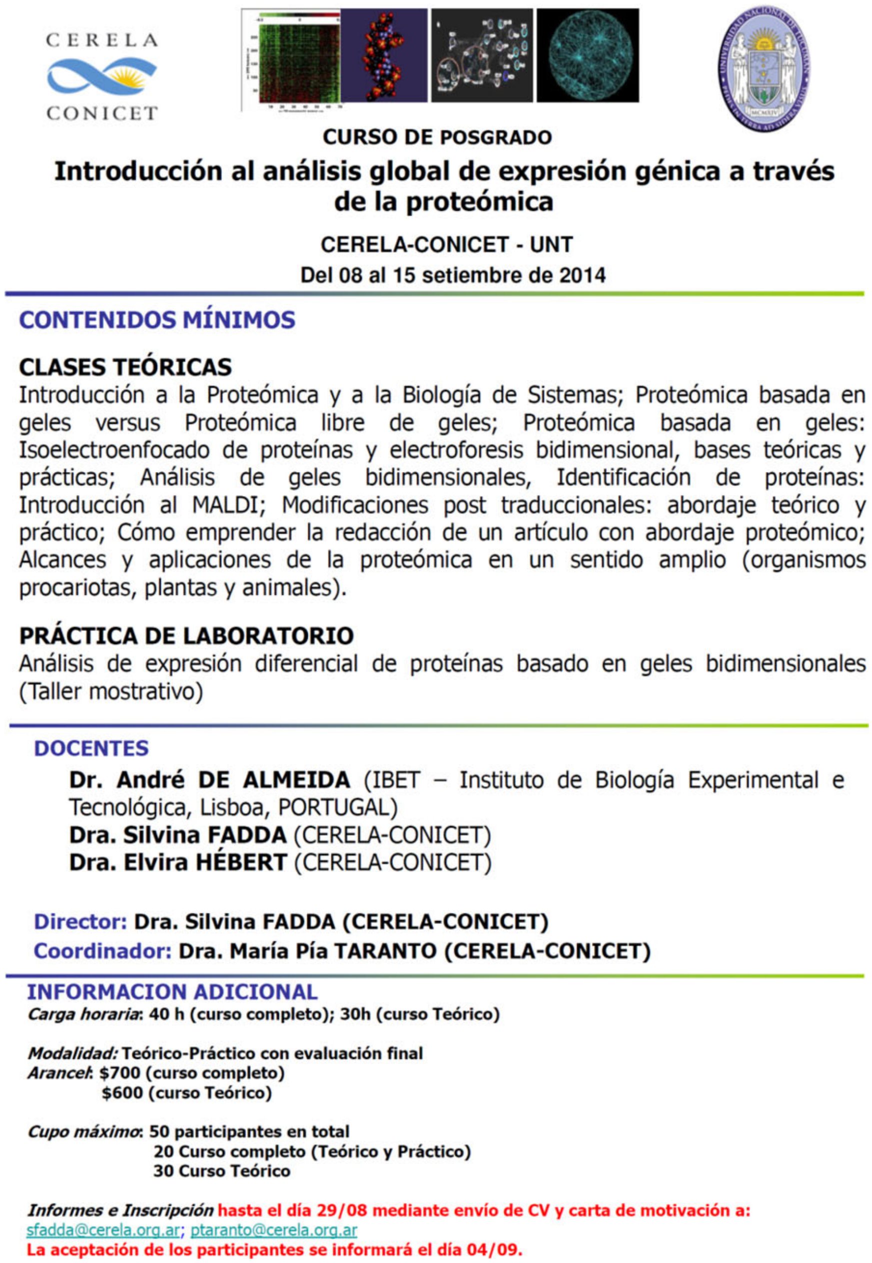

Figure 4. Poster of a Proteomics Introductory Course, part of a PhD program of the National University of Tucumán organized by the authors in September 2014 in the city of San Miguel de Tucumán.

participated in this course, revealing its usefulness for the countries in the Southern Cone with strong interactions between the Spanish and Portuguese speaking researchers and students.

The most recent Proteomics course held in CERELA-CONICET was organized by the two authors of this article during September 2014 (see poster of the course in Fig. 4). All students were Argentinean and worked for Argentinean institutions. Almost all students came from Northern Argentina with a particular relevance to those enrolled in PhD degrees from the National University of Tucuman. As such, the vast majority were PhD students in the early years of their degree, although there were five staff scientists and post-docs in a total of 40. The course was essentially devoted to 2DE and included both theoretical and practical classes. Students were introduced to theoretical concepts on Proteomics, 2DE, 2DE gel analysis and protein identification using Mass spectrometry, specifically using Matrix Assisted Ionization - Time of Flight MS and a small workshop on writing proteomics literature. The theoretical part of the course included also examples of applications of proteomics to research, particularly in the areas of Biotechnology, animal and veterinary sciences. The course included finally a practical part where students got acquainted with 2DE techniques and had the opportunity to follow the whole process: protein extraction and extract quantification, first dimension electrophoresis, second dimensional electrophoresis, gel staining, gel analysis software and spot excision. Students were asked to make a small presentation on how would proteomics fit in their research project and finally were evaluated with a standard multiple choice quiz. It was interesting to notice that the receptivity and interest of students in 2DE and in Proteomics in general was remarkably high. Additionally, it is important to mention that many of the students pondered using the technology to their specific research projects, which was one of the reasons provided for attending it.

5 Conclusions

From what was discussed previously, it is clear that Proteomics research is still in its infancy in Argentina. In fact, and although the bibliographic data place the country in a relatively good position within the Latin American or emerging nation contexts, it is clear that there is still a considerable effort to be made to bring Argentina to its rightful place as a regional scientific power. Therefore, such levels have necessarily to be closer to those of Europe, North America or Australia. This takes a considerable effort as the gap is without doubt large. Filling the gap would have to be accomplished through specific actions by both Argentinean researchers and academics, as well as science policy makers. The bottom line seems to go beyond the mere necessity for research funds. In fact, policies to attract or motivate proteomics researchers to stay in country, as well as additional efforts on bureaucracy curbing and training of future generations of proteomics researchers are a clear necessity. For the last 15 years, such an effort has been initiated by a resolute generation of Argentinean researchers. Patiently and against formidable odds, Proteomics has slowly been a presence in Argentina. The interaction with foreign research laboratories in Europe and North America, but also at the regional level of Southern Cone (Argentina, Brazil, Chile and Uruguay) have proven to be cornerstones in such effort. The examples are there. Areas like the Proteomics of bacteria of technological interest to the food industry within a broader context of farm animal proteomics has been an interesting study case of success. Equally, the appeal to young PhD students of Proteomics techniques seems to be a good indicator for the future of Proteomics in Argentina.

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