

**CV Stefan G Pierzynowski (SGP) 1951-02-12; Swedish citizen
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 Stefan.Pierzynowski@biol.lu.se; Stefan.G.Pierzynowski@gmail.com**

Name	Surname	Education/academic title/scientific degree
Stefan G	Pierzynowski	<p>1975, Veterinary Surgeon, Veterinary Medicine Faculty, Warsaw Agricultural University, Poland</p> <p>1982, Doctor of Veterinary Sciences (DVS), Veterinary Medicine Faculty, Warsaw Agricultural University, Poland. Thesis title "Conjugate effect of feeding and hormone agents on discharge of pancreatic juice in sheep". Supervisor – Professor W. Barej;</p> <p>1991, Doctor of Physiology (PhD), Dept Animal Physiology, Lund University, Sweden. Thesis title "Development and regulation of porcine pancreatic function with special reference to the exocrine pancreas". Supervisors - Assoc. Profs. B. Karlsson, B. Weström.</p> <p>Postdoctoral positions 1985 – 1991 Post-doc/Researcher, LU, Dept Animal Physiology, Sweden</p> <p>Qualification required for appointments as a docent/professor</p> <ul style="list-style-type: none"> - 1995, Habilitation = Docent (Doctor of Sciences), Veterinary Medicine Faculty, Life Science University, Warsaw, Poland. - 1995, Docent (Associate professor), Dept Anim. Physiology, Lund University, Sweden. - 1998, Adj. Professor, Cell and Organism Biology, Lund University, Sweden. - 2001, Full Professor, Veterinary Sciences, Faculty Veterinary Medicine, Warsaw Agricultural University, Poland. <p>Professor Stefan Grzegorz Pierzynowski in 2001 received the title of full professor at the Faculty of Veterinary Medicine at the University of Life Sciences (SGGW). In the years 2004-2013 he served as Head of R&D Esentys AB Ideon Science Park, Lund, Sweden. Since 2008 is a professor / researcher at the Department of Biology at Lund University, and since 2009 he has been a visiting professor at the Department of Medical Biology at the Institute of Medicine in Lublin.</p>

Position

Professor - Member of the Investment Committee, Chairman of the Scientific Councils

Professional experience in the field of investment, raising subsequent rounds of financing and disinvestment

*For over 20 years he is related with investment activities, within which he realized approx. 7 investments in companies such spin-off, with a total commitment of capital in the **amount of 10 mln PLN** In 2001-2015 he commercialized approx. 3 of his solutions. He has experience in acquiring a second round of funding and disinvestments. **In 2010-2015 led the process of approx.2 disinvestments reaching 500% return on investment.** He sold about approx. 20 patents in the total amount exceeding 20 mln PLN.*

*Experience in conducting the entire transaction process of **disinvestment for his own companies.** conducted a capital entry selling his shares to outside investors, other shareholders.*

As a person acting on the capital market participated in:

- *establishment of personal and capital companies,*
- *designing their equity- share structure*
- *analysing and designing business ideas subject to financing,*
- *negotiating provisions of investment contracts and determination of structures of purchase and sale of the portfolio companies,*
- *analyses of due diligence preceding capital investments,*
- *investment and management decision making,*
- *making investments and disinvestments in the companies of SME sector in return for a cash contribution.*

In 2002, Stefan Pierzynowski conducted a capital entry into the company SGP&Sons AB. The leading profile of the company SGP&Sons AB was research - development activity, as the result of which several patents in the borderland of medicine and biology were produced. In 2006, the transaction of disinvestment was conducted (exit) through the sale of shares in the SGP, to the company of Essentys AB. In return, Stefan Pierzynowski received fixed remuneration for the transferred shares and a 10% of shares in Essentys.

The next stage of the investment process was the disinvestment from the company Essentys and the entry to the capital of Grespo AB company (in return for of 9.36%). As part of the research - development activity Professor Pierzynowski contributed to the patents development that were ultimately commercialized.

He has the knowledge and practical skills: project management taking into account the financing of projects and enterprises, identifying the needs of projects (time, resources, budget) implementation of the procedures of due diligence and measures related to the operation and management of customer relations.

Professional experience in the acquisition and commercialization of R&D projects or conducting R&D projects

Professor Stefan G Pierzynowski has extensive experience in conducting R&D, sourcing and preparation of investment projects of research - development character in the early stages of development, as well as their conduct and commercialization.

Professor Stefan Grzegorz Pierzynowski in 2001 received the title of professor at the Faculty of Veterinary Medicine at the University of Life Sciences (SGGW). In the years 2004-2013 he served as Head of R&D Esentys AB Ideon Science Park, Lund, Sweden. Since 2008 is a professor/researcher at the Department of Biology at Lund University, and since 2009 he has been a visiting professor at the Department of Medical Biology at the Institute of Rural Medicine in Lublin.

The main **scientific and professional achievements** of Mr. Stefan G Pierzynowski include among others:

1. detection and description of the regulation of separation of the pancreas in the way of CCK-dependent short arcs,
2. description and patenting of several biological functions of alpha-ketoglutaric acid, for example anti-osteoporotic effect, reduction of LDL levels, increase flexibility of blood vessels, the anticancer properties, etc.,
3. description of the assimilation factor (favouring obesity), allowing for assimilation of the absorbed elementary diet components,
4. ability of organization of biomedical studies in humans (studies of clinical phase I - III) and animals in

accordance with the principles of GLP and GCP,

5. skills in management of small and average size of R&D plants.
6. Development of several animal models for innovative studies e.g., exocrine pancreas insufficiency pig model to study formulas effect on term and preterm neonates growth and development.

Professor Pierzynowski has extensive experience in conducting R&D projects (realization of basic research and industrial development, creation of new solutions, innovative in the world scale) and the commercialization of R&D projects (creation of market analysis on the possibility of the development of innovative technological solution or product / service and/or its commercialization and technology transfer. This is evidenced by the completed research and industrial grants: Mr. Stefan G Pierzynowski realized several research and industrial grants, including:

7. FORMAS, 1998-2002 (2 million SEK) - **Chief researcher - contractor of the project.** The regulation of the pancreas secretion and its influence on the growth of newborn animals.
8. Swedish Institute, 2003-2006, Visby Program, Network; Ukraine – Belarus - Sweden: (0.6 MSEK) - **Project Coordinator** - Probiotics for good or worse: translocation of lactic acid bacteria (LAB) DNA to the cells of the host tissues (Probiotics: translocation of DNA of lactic acid bacteria to the cells of host tissue)
9. EUREKA; Healthy-Weaning, 2002-2004 (1 mln SEK). **Originator. Chief coordinator of the** Polish-Swedish **project**, whose product was a patent. Currently the patent is commercialized by Biotek company. Healthy weaning of offset piglets is a fact.
10. EUREKA; Healthy-Weaning, 2002-2004 (0.8 mln SEK). **Originator.** Polish Swedish project - Swedish coordinator. The idea is commercialized by feed mills, "Morawski", Kcynia, near Bydgoszcz
11. Vinnova - ERA-Net Transnational Call, 2008 - 2011 (3.5 mln SEK). **Originator and the project coordinator** on the Swedish side. The properties of nano-alpha - keto glutarate (AKG). AKG is recognized as a molecule of life. A patent application was created.
The end results is the technology of bioactive nano - diamond carbon powder, guidelines for the development of feed mixtures produced on the basis of powders produced and the technology of obtaining a new product based on carbon powders and AKG included in the confidentiality clause. Research on anti carcinogenic combination of carbon powders and AKG are a very important part of the project dedicated to the company Essentys AB.
12. SI 2010-2013, Visby Program, Network; Ukraine –Sweden (0.6 mln SEK). **Originator and coordinator of the project.** Study on an novel nutrient assimilation factor (NAF) with potential to influence obesity. From (Studies on the novelty factor of assimilation of the nutritive substances with the possibility of influencing obesity)
13. FOFIND - EU Grant (2012- 2015)– 400 thou. EUR . RTD provider. Development and human validation of new healthier food products using low-cost functional ingredients”. (Development and confirmation of new, healthier food products using cheap functional ingredients)
14. Gramineer Int. AB (1998 – 2002), 25 mln SEK. **Originator** for all patents for Gramineer AB.
15. Solvay Pharmaceutical GmbH (2001-2002), Hannover, Germany, 1 mln SEK. **Project Head.** Investigation of lipase non-absorption/absorption after oral administration of Creon 10.000 MMS in the pig by Karin Gewert, Scott Holowachuk and Stefan Pierzynowski. (Investigation of lipase non-absorption/absorption after oral administration of Creon 10.000 MMS in the pig by Karin Gewert, Scott Holowachuk and Stefan Pierzynowski).
16. Arexis AB (2004), Sverige, 0.5 mln SEK Project Head. Relation between pH in the stomach, BSSL

formulation and BSSL activity in the stomach and in the duodenum (Relation between pH in the stomach, BSSL formulation and BSSL activity in the stomach and in the duodenum).

17. Arexis AB (2005), Sverige, 2.0 mln SEK **Project Head**. The effect of lipase substitution in pancreatic duct ligated pigs: effect on coefficient of fat absorption (CFA) (The effect of lipase substitution in pancreatic duct ligated pigs: effect on coefficient of fat absorption).
18. Addisseo SAS (2008), France (100 thou. USD). **Originator. Project Head**. Integration of an *in vivo* technique, designed to measure the “language of muscle” – electromyography, with both feed and blood methionine levels. (Integration of an *in vivo* technique, designed to measure the “language of muscle” – electromyography, with both feed and blood methionine levels)
19. Alnara Pharm Ltd (2007–2009), USA/SGPlus, Sweden (1 mln SEK). Originator, Project Director.
20. Essentys AB (2003– 2013) donating to BI, LU 30% of employment time for SAP (donating to LUND 30 % of the employment time SAP), 20 thou. SEK/month. Beneficiary. Donation of the paid work time SGP to any life science studies carried out by the SGP with booking and the precedence to purchase of the results.
21. Essentys AB (2003–2012) allocated for SGPs Research 50 thou. SEK/month (devoted to SGP studies 50 thou. SEK a month). Beneficiary. Donation of money to any life science studies carried out by the SGP with booking and the precedence to purchase of the results.
22. Vitanano /Allena Ltd/Alcresta Ltd (2012 – 2015), 60 000 USD (PhD scholarship), research grants 500 thou., USD. **Originator**. Director of several projects, including graduate students. Research on medical devices to digest fats in formulas for premature babies.

Professor Stefan Pierzynowski was on behalf of Lund University Commissioned Education (LUCE), coordinator of the program "TransFormation.doc", which was carried out in the framework of the system project of the Ministry of Science and Higher Education "Support for the management of scientific research and its results", financed by the Operational Programme Innovative Economy. Within the project 2-week courses for 200 doctoral students and young researchers (10 groups of 20 people) was organized in LUCE.

Classes within the course included lectures, workshops, panel discussions, study visits, role-playing, simulation games and creative thinking techniques. Participants also visited the medical complex, business incubators and got familiar with the Swedish system of science, business and support for students and young entrepreneurs. The participants' tasks was to prepare and pre-develop three business ideas related to research. Scientists were working on projects individually and in groups during the entire stay at the University of Lund. In addition, researchers presented their best work based on the business model NABC. The model is a tool for the creation, evaluation and presentation of ideas, can be used in everyday situations. The method was developed in the USA by members of the Stanford Research Institute. During the training young scientists exchanged their experience in interdisciplinary teams. Members of the groups represented medical, chemical, biological, veterinary, technical, economic, social and humanistic sciences. Participants pooled their research interests with the business world. Contacts established between a group of graduate students and young scientists from Poland and international environment allowed for the exchange of information within the networking and interdisciplinary research and commercialization.

Professor Stefan Pierzynowski as a manager was responsible for issues related to budgeting, involvement of the personnel conducting different types of activities, the logistics of the project, the organization of transport, accommodation, additional activities, etc .. At the same time he gave classes in the course:

- presentation of Lund University
- Swedish innovation system - the presentation of the structure of innovation in Sweden, the Swedish experience, the role of the agency of innovation systems
- Patents - how it works (lecture and seminar), why you should protect your invention, the patent system in a short, what types of inventions can be protected by patent, how to apply for a patent

Professor led the implementation studies for the industry and has worked with: Essentys AB, Sweden; Nutreco BV, The Netherlands; Culinar AB, Kristianstad, Sweden; Solvay Pharmaceutical GmbH, Hannover, Germany; Danone, Paris, France; Biovitrum AB, Stockholm, Sweden; Lantmänen, Malmö, Sweden; Adisseo, France; AlnaraPharm, Boston, USA; Alcresta Boston, USA; Allen Ltd, Boston, USA.

The portfolio of Professor Stefan G Pierzynowski consists of more than **500 publications** and **25 patents and patent applications**.

SELECTED PUBLICATIONS:

1. Pierzynowski S, Ushakova G, Kovalenko T, Osadchenko I, Goncharova K, Gustavsson P, Prykhodko O, Wolinski J, Slupecka M, Ochniewicz P, Weström B, Skibo G. Impact of colostrum and plasma immunoglobulin intake on hippocampus structure during early postnatal development in pigs. *Int J Dev Neurosci*. 2014 Jun;35:64-71.
2. Goncharova K, Pierzynowski SG, Grujic D, Kirko S, Szwiec K, Wang J, Kovalenko T, Osadchenko I, Ushakova G, Shmigel H, Fedkiv O, Majda B, Prykhodko O. A piglet with surgically induced exocrine pancreatic insufficiency as an animal model of newborns to study fat digestion. *Br J Nutr*. 2014 Dec;112(12):2060-2067.
3. Goncharova K, Skibo G, Kovalenko T, Osadchenko I, Ushakova G, Vovchanskii M, Pierzynowski SG. Diet-induced changes in brain structure and behaviour in old gerbils. *Nutr Diabetes*. 2015 Jun 15;5:e163.
4. Liudmyla Lozinska, Björn Weström, Olena Prykhodko, Andreas Lindqvist, Nils Wierup, Bo Ahrén, Katarzyna Szwiec, Stefan G. Pierzynowski. Decreased insulin secretion and glucose clearance in exocrine pancreas insufficient pigs. *ExpPhysiol*101.1 (2016) pp 100–112.
5. Pierzynowski SG, Goncharova K, Woliński J, Prykhodko O, Weström B, Lozinska L. Enteral pancreatic-like enzymes of microbial origin affect insulin release during an intravenous glucose tolerance test. *J Diab Met*, 7: 681. doi:10.4172/2155-6156.1000681, 2016

SELECTED PATENTS AND PATENT APPLICATIONS:

6. Pierzynowski S., Prykhodko O., Weström B. Gut – Maturation- Enzymes. Swedish patent application PM30142US00 , 2010.
7. Pierzynowski, S.G., *PCT/SE2013/051098 - patent application*. 2013 COMPOSITIONS USEFUL AS MEDICAMENTS . Field of the invention. The present invention relates to the field of medicine and nutraceuticals, in particular the treatment of disorders involving eosinophilia, neurological and/or neurodegenerative disorders and improvement of brain function.
8. Pierzynowski SG and Goncharova K To combat insulin resistance/obesity with amylase derived peptides Patent application: SE 1551220-5 (2015-09-23) and EPO 16172416.6 (2016-06-01)

Professor Stefan Pierzynowski cooperated and cooperates scientifically with several universities, research institutes:

Universities / Institutes

- Dept Agricultural Biosystems and Technology, Swedish University of Agricultural Sciences at Lund and Alnarp, Sweden (Prof. J Svendsen, Drs. D Rantzer, J. Bortemans – pancreas vs. growth)
- Dept Medicine, Lund University, Lund, Sweden (Prof B Ahrén – regulation of insulin realising)

- Dept Medical Microbiology Dermatology and Infection, Lund University, Sweden (Prof Å Ljungh, DSc D Kruszezwska – LAB vs. gut function)
- BMC; Dept Cell and Molecular Biology, LU, Sweden (Assoc. Prof. Charlotte Erlanson-Albertsson - functional food – thylakoides, pancreas regulation)
- Clinical ReserchCenter; MAS Malmö, Sweeden (Bariatric surgery – metabolic surgery; Prof. Leif Groop, Dr. Nils Wirup)
- Dept Animal Nutrition, and Physiology, Danish Institute of Animal Science, Foulum, Denmark. (Drs M S Hedeman, NB Kristensen, Ch Lauridsen, H Laerke – AKG biological effects, pancreas function and regulation – functional food)
- Dept Anatomy and Physiology, Royal Veterinary and Agricultural University, Copenhagen, Denmark (Prof. A Harrison – blodd vessels elasticity vs. AKG)
- Research Institute for the Biology of Farm Animals, Dummerstorf. Germany (Assoc Prof W Souffrant – stabile isotopes)
- Institute of Animal Nutrition, Hohenheim University, Stuttgart (Prof. R Mosenthin – SCFA vs. ileal brake and exocrine pancreas function)
- Dept Animal Nutrition, Wageningen University, The Netherlands (DrJ van der Borne insufficiency of exocrine pancreas for growth)
- The Kielanowski Institute of Animal Physiology and Nutrition, Poland (Gut remodeling in neonates, Drs. J Wolinski, M Sluoicka)
- Dept Animal Physiology, Vet Med Fac., Lublin Agricultural University. (Profs. S Winiarczyk and J Valverde Piedra – regulation of bile and pancreas secretion, Bariatric surgery vs. keedney stones development – pig model)
- Inst Agricultural Medicine, Lublin, Poland (Dr R Filip - osteoporoses)
- Dept Animal Physiology, Warsaw Agricultural University, Poland (Dr P Podgurniak - regulation of gut function and development)
- Institute of Biochemistry and Biophysics, Warsaw, Poland (Prof.EGrzesiuk – bacteria growth vs. MMC)
- Children’s Nutritional Research Centre, Baylor College of Medicine, Huston, TX, USA (Prpf. D Burrin – amino acid absorption)
- E (Kika) de la Garza Institute for Goat Research, Langston, OK, USA (Prof. T Sahlu, AssocProf. R Puchala – nutritional peptide tissue utiliastioin)
- Dept health and Sort Sciences Memhpis University, TN, USA (AKG vs human health, Prof. R Buddington)
- School of Physiology, University of the Witwatersrand, Johannesburg, South Africa (Dr. K H Erlwanger – AKG vs. elderly)
- Laboratory of Physiology, Graduate School of Environmental Sci.and Institute for Environmental Sciences, University of Shizuoka, Japan (Prof. A Kuwahara – cancer vs. environment)
- Dept Chemistry , University of Trás-os-Montes e Alto Douro, Portugal (Prof. F Nunes – chemistry of the carcinogenic substances)
- Dept Microbiology and Virology (UMCS - University Maria Curie Skłodowska), Lublin, Poland (Profs. M Kandefer-Szerszeń, W Rzeski - molecular biology)
- Dept Veterinary Medicine, RakunoGakuen Univ., Ebetsu, Hokkaido, Japan (Prof. S Kato- exocrine pancreas regulation)
- Dept Biophysics and Biochemistry, Faculty of Biology and Ecology, Dniepropetrovsk National University, 13 Naukova Str., Dniepropetrovsk 49050, Ukraine. (Prof G Ushakova – brain proteins vs. LAB)
- Dept Experimental Hepatology, Institute of Biochemistry, National Academy of Sciences, Tarashkevich (BLK) Boulevard, 50230017 Grodno, Belarus. (Prof. V. Buko - liver dysfunction)
- Dept Cytology, Bogomoletz Institute of Physiology, Bogomoletz street 4, 01024, Kiev, Ukraine (Prof. G Skibo – brain ischemia)
- Department of Biochemistry and Biotechnology, VassylStfanykPrecarpathian National

University, 57 Shevchenko Str., Ivano-Frankivsk, 76025 Ukraine. (asimilin – obesity facto
Prof. V Lushchak, G Semchyshyn)

This cooperation focuses on creating the concept of scientific solutions in technology, products, and research patentability, assessment of the usefulness of technology, state of the art, protection of industrial property and technology transfer.

Additionally, he is an active member of many professional organizations, academic and research: Polish, Swedish and international, such as:

9. European Pancreatic Club (EPC) - since 1986
10. Polish Physiological Society (PPS) - since 1985
11. American Zootechnical Society (ASAS) - since 1992
12. International Association of Veterinary Specialists in the Pigs (IPVS) - since 1986
13. Polish Physiological Society (PPS) - since 1975

The professor has worked as an expert for the European Union on Polish and foreign programmes:

14. PHARE Projects- *animal nutrition and GLP expert: Quality management in the dairy sector - P 0312-05-01 (1995/97)*;
15. Promoting agriculture friendly towards aquatic environment in individual farms in the Bug-Narew basin (Ostrołęka and Olsztyn, research, education) P105/93 (1996-1997); Determination of a prolonged broad strategy of environmentally balanced agriculture - P9312-06-02 (1997-1998);
16. *Running and developing dairy farms to enhance rational use of basic production inputs (labour, land, capital, management)*, (ZROW/700/00001/2002/FAPA)
17. Chief 1998 – 2000 COST 98 - EU "Effects of antinutrients on the nutritional value of legume diets"

Professor is also a reviewer of scientific journals: *Peptides, Digestive Diseases and Sciences, Journal of Animal and Feed Sciences, British Journal of Nutrition, Journal of Nutrition, Experimental Physiology, Journal Nutrition, Journal Animal Science*, as well a reviewer of books: *Metabolic stress in dairy cows. 1999, Eds. Oldham et al., Nutrition and health of the gastrointestinal tract. 2002, Eds. Block et al.* In addition, Mr. Stefan Pierzynowski is the editor of professional journals: *Livestock Science – Elsevier I Journal of Preclinical and Clinical Research (IMW, Lublin)*.

Summing up the achievements in research-development it should be noted that Professor Pierzynowski has experience in projects involving R&D work on innovative solutions, which resulted in the implementation of the results of R&D to business, acquired patents and rights of protection for utility models or other uses of the results of R&D works. In the course of R&D projects, he also performed analyses of due diligence in terms of the risks of technology, product, legal, market and state aid.

Thanks to international cooperation with scientific institutions, Professor Stefan Pierzynowski speaks five foreign languages, including:

18. Polish - mother tongue
19. Swedish - fluently
20. English - fluently
21. Russian - good
22. German and Danish - fair

The role in the Grant Project

Professor Pierzynowski will act as Chairman of the Scientific Council and will be a member of the Investment Committee. As part of his function his role primarily will focus on:

- Cooperation with a team of business analyses and Scientific Council.
- At the stage of the selection of projects he will lecture to the participants of the Scientific Circles and Associations, dealing with the field of medicine and biotechnology his knowledge in this field, and also obtain contacts for the most talented students, having interesting ideas for business.
- Performing analyses of due diligence in terms of the risks of technology, product, legal, market and state aid.
- Participation in the decision-making process and the key investment decisions in the cases when this is required.
- Participation in the evaluation aimed at withholding assistance to Grantees, when at the stage of Proof of Principle phase the received test results or external analyses and opinions are negative or the financial and legal analysis indicate at the lack of the project implementation possibility by the team of Aligo VC
- Performing obligatory duties in accordance with the current regulations, Committee resolutions, the terms of the Grant Agreement and the rules of the fund functioning.
- Participation in the implementation of the strategy of investment and disinvestment indicating several possibilities of ending capital commitment in the companies.
- Creating, developing terms and provisions of the investment agreement at the stage of proof of Concept

Involvement in the Grant Project (hours/week)

40/h/week

Grants

Research grants (2002–2015)

- FORMAS, 1998-2002 (2 millions SEK)
- Swedish Institute, 2003-2006, Visby Program, Network; Ukraine – Belarus - Sweden: (0.6 million SEK)
- EUREKA; Healthy-Weaning, 2002-2004 (1 million SEK)
- EUREKA; Lab-Diets, 2002-2004 (0.8 million SEK)
- Vinnova - ERA-Net Transnational Call, 2008 - 2011 (3.5 million SEK)
- SI 2010-2013, Visby Program, Network; Ukraine –Sweden (0.6 million SEK)
- FOFIND - EU Grant (2012- 2015)– 400 kEuro

Industrial grants (2002–2015)

- Gramineer Int. AB (1998 – 2002), 2.5 million SEK
- Solvay Pharmaceutical GmbH (2001-2002), Hannover, Germany, 1 million SEK
- Arexis AB (2004), Sverige, 0.5 million SEK
- Biovitrum AB (2005), Sverige, 2.0 million SEK
- Addisseo SAS (2008), France (100 000 USD)
- Alnara Pharm Ltd (2007–2009), USA/SGPlus, Sweden (3 million SEK)
- Essentys AB (2003– 2013) donating to BI, LU 30% of employment time for SGP, 20 000 SEK/month
- Essentys AB (2003–2012) allocated for SGPs Research 50 000 SEK/month
- Vitanano /Allena Ltd/Alcresta Ltd (2012 – 2015), 60 000 USD (PhD scholarship), research grants 600 000 USD.

Examples funded projects

Project 1

Name of the funded project:

Kind of the project:

Date of Support:

<p>The level of specific proteins of neurons in different areas of the brain of a pig with exocrine pancreatic insufficiency (EPI) treated with a pancreatic-like enzyme mixture (PLEM). Department of Biology, University of Lund</p>	<p>Industrial <input type="checkbox"/></p>	<p>R&D <input checked="" type="checkbox"/></p>	<p>2011-2012</p>
<p>Value of the given support</p>	<p>The value of support from private funds (in EURO)</p>		<p>The value of support from public funds (in EURO)</p>
<p>140 000.00</p>	<p>140 000.00</p>		<p>0.00</p>
<p>Project description</p>			
<p>Acute and chronic pancreatic insufficiency is often associated with significant neurological changes associated with cognitive and sensory functions. However, still missing is a detailed study of the brain in these conditions in animal models (especially pigs).</p> <p>The distribution of specific proteins in neurons (neural cell adhesion molecules - NCAM), the major basic protein - MBP fibrillary acidic protein - GFAP and calcium binding protein S100B) in the four areas of the brain of a pig with exocrine pancreatic insufficiency was investigated. The data obtained revealed that pancreatic insufficiency results in progressive damage to neurons that were most marked in the hippocampus and then in the thalamus and cerebellum. Neuronal damage is the most visible through a significant decrease in neuronal membrane adhesion molecules and the main basic protein (notably in the thalamus), which leads to insufficient synaptic plasticity. In addition, the decreasing level of the MBP protein in the thalamus is correlated with an increase of protein level in the blood plasma.</p> <p>Furthermore, a close relationship was observed between the neuronal damage and activation of GFAP and the level of protein S100B (astrocyte specific protein) in various brain areas under exocrine pancreatic insufficiency condition (hippocampus is the most vulnerable region in the brain of pigs with exocrine pancreatic insufficiency).</p> <p>Treatment with pancreas-like enzymes = PLEM for 10 days (8 capsules/pig/day) prevents future degenerative processes and makes it possible to restore the main parameters studied.</p>			
<p>Justification of the research and development nature</p>			
<p>The effect of PLEM at S100B level in the hippocampus and cerebellum should be further examined (dosage and time), because at the moment it cannot be determined whether the effect will be good for the brain or beneficial after treatment.</p> <p>All these observations indicate that (a) chronic pancreatic insufficiency is able to selectively induce neuronal, glial cells and myelin lesions in the brain of pigs depending on the area, (b) treating with PLEM is capable of preventing a future neurodegeneration. These observations strongly suggest that the model EPI can be used to search for new therapeutic agents to increase neuronal regeneration in chronic pancreatic insufficiency.</p>			
<p>List of research and development works in the project with an indication of their value</p>			
<p>Industrial research carried out under the project</p>			
<ol style="list-style-type: none"> 1. Development of the optimal composition of (formulation) of enzymes and forms of administration (capsule) 2. Studies on the prototype capsule and matrix opening in the intestine rather than the stomach and containing coated and matrixed - resistant to dissolution in the stomach granules of the matrix with 			

enzymes. The value of IPR and patent application is at least 2 million PLN

Industrial research carried out under the project

- 1. Developing of the fat matrix protective for enzymes.*
- 2. Developing of the cross-link of enzymes increasing its resistance to digestion in the stomach*
The value of IPR in patent application is at least 1 million PLN

The role played in the process of project funding

Sponsor and Project Director

Funded projects

Project 2

Name of the funded project:	Kind of the project		Date of support
<i>Development of a model of chronic kidney disease (CKD) and hyperuricemia in young pigs. Kielanowski Institute of Animal Physiology and Nutrition, Jabłonna, Poland</i>	Industrial <input type="checkbox"/>	R&D <input checked="" type="checkbox"/>	2015 - 2016
Value of the given support	The value of support from private funds (EURO)	The value of support from public funds (in EURO)	
150 000.00	150.000,00	0.00	

Project description

Uric acid is the final product of purine metabolism in humans. The average concentration of uric acid in human blood is 6.8 mg/dL. In healthy humans, uric acid is excreted in the urine. However, the excretion of uric acid can be reduced by kidney disease, which can lead to hyperuricemia. Hyperuricemia is defined as the level of uric acid in the blood above the normal range, and may be the result of problems with the excretion of uric acid due to renal dysfunction or increased production of uric acid. In addition, a diet high in purine and fructose, as well as exposure to lead, may also contribute to high levels of uric acid. Hyperuricemia leads to gout, and kidney stones.

Most mammals have low levels of uric acid due to the presence of the enzyme uricase, which catalyses the oxidation of uric acid to a more soluble allantoin. However, the presence of uricase has been lost in humans and higher primates as a result of a mutation in exon 2 in the course of evolution. Therefore uricase from various microorganisms has been used intravenously for nearly 40 years for treatment of hyperuricemia and gout in humans. However, the clinical use of multiple preparations of uricase has been limited due to their undesirable biological properties (i.e. the premature decomposition and deactivation of endogenous protease, elimination of the reticuloendothelial system, and the immunogenicity and the toxic side effects caused by the immune reaction to foreign protein).

Swine models have proven useful in a variety of disease processes and medicine test because of the anatomical and physiological similarities to man and the extrapolation of the discovery for clinical conditions. Previously, hyperuricemia has been studied in mice, a model pig tests were not carried out until today.

The primary objective of the study was to develop a stable model of CKD (stage 3-4) and hyperuricemia in pigs caused by infusion of uric acid (urate target level of 5-6 mg/dL plasma) and oral tests of uricase.

Justification of the research and development nature

- 1. The main goal of this study was to create a stable model of CKD (stage 3-4) and hyperuricemia in young pigs (target levels of uric acid 5-6 mg/dL plasma)*
- 2. An additional aim was to examine the relationship between hyperuricemia and hyperuricosuria in the model and investigation of the action of tablets containing uricase.*

List of research and development works in the project with an indication of their value

Industrial research carried out under the project

1. development of enzyme composition and a vehicle for tablets with uricase, value of approximately 500 thousand PLN

Industrial research carried out under the project

1. Proving the existence of a critical level of uric acid in the blood from which the acid begins to be metabolised in the gut / passes into the intestine where it can be metabolised by uricase administered in a tablet! . Scientific value

The role played in the process of project funding

Sponsor and Project Director

Funded R&D projects

Project 3

Name of the funded project:	Kind of the project		Date of support
<i>Investigation of the safety, tolerability and efficacy of enteral feeding with a mixture of hydrolysed milk for premature infants PREFIC in a pig model with the immaturity of the gastrointestinal tract and pancreas - studies of the future intended use in the treatment of premature infants.</i> Department of Biology, University of Lund	Industrial <input type="checkbox"/>	R&D <input checked="" type="checkbox"/>	2015 - 2016
Value of the given support	The value of support from private funds (Euro)	The value of support from public funds (in PLN)	
250 000.00	250 000.00	0.00	

Project description

Long-chain polyunsaturated fatty acids (LCPUFA) are important in early development, particularly the neurophysiological development, however, PUFA acids are poorly digested and absorbed especially in premature infants with progressive exocrine pancreatic insufficiency. Absorption of LCPUFA, especially omega-3 and omega-6 (FA), is essential for growth and development, along with the most important cardio-vascular, visual and cognitive health benefits over the human life. However, it is weak in premature babies or term infants who were formula-fed with milk. The main cause of this poor absorption and insufficiency of LCPUFA is exocrine immaturity of pancreas and gastrointestinal (GI) tract. In order to improve the digestion and absorption of fats and reduce the shortage of long-chain polyunsaturated fatty acids PUFA, infant formulas composition resembled mother's milk and have been supplemented by the most important PUFA fatty acids (DHA, AA, LA). However, plasma concentrations were lower than in breastfed infants. Unlike the protein, which may be provided in the form of peptides, the fats contained in the formula are in a stable form of triglycerides, which must be hydrolysed by pancreatic lipase to fatty acids and monoglycerides prior to absorption and utilization in the body.

PREFIC is a carrier of digestive enzymes, which is currently under development at Alcresta, matching the system of feeding infants receiving enteral feeding by nasogastric or oro-gastric tube. PREFIC consists of immobilized lipase (iLipase), which hydrolyses fats, when the mixture is passed through the tube, providing digestible fatty acids, including the most complex PUFA such as EPA and DHA, to the gastrointestinal tract. The immobilized lipase is retained in the carrier, and only the hydrolysed mixture is consumed. This has been specifically designed to optimize the benefits of enteral feeding and providing more fat and reduce the shortage of critical LC-PUFA. PREFIC is the second use of immobilized lipase by the company Alcresta. EFIC or Relizorb is a larger version of the immobilized enzyme carrier designed for 500 mL enteric mixture. EFIC is currently under approval by the FDA.

For the purposes of this study, PREFIC is equal to EFIC. Currently, the device EFIC (Relizorb) will be used for testing in this study. PREFIC device will be a smaller version of the device EFIC to accommodate the

smaller quantities and to provide more frequent feeding in the population of premature infants, hence for this study EFIC device is a prototype version of the device PREFIC. The use of a prototype PREFIC means 10X exposure to the active ingredient (iLipase) than would be experienced by premature babies. This estimate assumes 8-10 feedings a day using the device PREFIC containing 100 mg of iLipase in each feeding (total exposure of 1 g per day).

The active ingredient of prototype PREFIC is commercially available in the form of bacterial lipase from *Rhizopus oryzae* (RO Lipase) immobilized on acrylic beads and placed in a single, sterile medium, which is connected in one line with a feeding set. The acrylic bead is classified as a substance that may have contact with food, a complex with lipase (iLipase) is approved for adults and paediatricians by the FDA (FCN 1498).

PREFIC prototype is designed in such a way as to mimic the action of pancreatic lipase by the hydrolysis of triglycerides into their absorbable form of free fatty acids and monoglycerides in the feed mixture containing all formulations provided by enteral feeding.

Therefore, we postulate that preterm infants fed with the hydrolysed PREFIC in the formula for preterm infants (IF) or pasteurized milk (DM) have improved absorption of fat and specific PUFAs such as DHA, ALA, LA, AA, essential for the growth and development and, due to insufficient dietary fat absorption symptoms can be reduced.

It is known that at the functional level humans and pigs have many similarities in the digestive, urogenital and cardiovascular system. It has also been demonstrated that the growth time and cerebral metabolism of PUFA is very similar. What important, the pig model of born prematurely has anatomical, physiological, immunological and metabolic similarity to human infants. Key features of premature pigs concern size (e.g. 0.6-1.1 kg), the immaturity of the gastrointestinal tract, and the respiratory, nutritional, immunologic and metabolic disorders after premature birth.

Therefore, in order to examine the safety, tolerability and efficiency of PREFIC as part of enteral feeding for prematurely born infants, we prepared the study on prematurely born piglets that resemble human babies at 32 weeks of gestation. What important, the piglets born prematurely are missing 70% of the exocrine function of the pancreas, and the gastrointestinal tract is immature, as in the case of human neonates, where PREFIC is intended for use.

Justification of the research and development nature

The study (prepared without the requirements of GLP) was carried out in two parallel groups:

1. The control group fed with non-hydrolysed formula for prematurely born babies (n=8+2)
2. Group PREFIC fed with hydrolysed formula for prematurely born infants in the form of fatty acid and monoglycerides (n=8+2)

The safety, tolerability and absorption of fat and fatty acids including LC-PUFA will be tested in the study divided into two parts:

1. A short 24-hour kinetic study, where IF ± PREFIC - enteral feeding every two hours for 24 hours
2. A longer 7-day study in prematurely born pigs, where IF ± PREFIC will be administered every two hours for 7 days

The main objective:

The main purpose of the short study was to show that the administration of digestible fats in the form of fatty acids and monoglycerides (when exposed to PREFIC) is safe and does not cause disorders such as diarrhoea, vomiting and bloody stool, etc.

Secondary objective:

An additional aim was to investigate the absorption profile of a fatty acid with a long chain (LC-PUFA), mainly AA, DHA, ALA, LA during the initial 24-hour of feeding with IF±PREFIC expressed as relative or concentrated changes in plasma, but also as a loss of fatty acids in the stool and/or a change of the specific absorption factor of the fatty acid.

List of research and development works in the project with an indication of their value
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Industrial research carried out under the project
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<i>Development of a prototype column with immobilized enzymes digesting fat - the commercial value - from 1 to several million PLN</i>
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Industrial research carried out under the project
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| <ul style="list-style-type: none">– <i>selecting the proper enzymes and the exposure time. Patent application. Value from 0.5 to several million PLN.</i>– <i>total value of industrial and development research exceeds the unit value and is at least 3 million PLN.</i> |
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The role played in the process of project funding
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<i>Sponsor and Project Director</i>
