CURRICULUM VITAE

Georgia Sotiropoulou

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E-mail: gdsotiro@upatras.gr Research: https://skink5.gr/#
http://www.pharmacy.upatras.gr/index.php/en/research/laboratories/61
http://www.pharmacy.upatras.gr/index.php/el/research/labs/61
AND Affiliated Investigator, Biomedical Research Foundation,
Academy of Athens E-mail: gdsotiro@bioacademy.gr
http://www.bioacademy.gr/faculty-details/HMmM/gewrgia
2014, Visiting Professor, *Imagine* Institute INSERM UMR 1163,
University Hospital Institute, Université René Descartes Paris 5-Sorbonne
Paris Cité, Paris, France

Public Profiles

Google Scholar: https://scholar.google.com/citations?user=Rlk1ntkAAAJ&hl=el&oi=ao&user=2Jbk6IcAAAAJ
Research Gate: https://www.researchgate.net/profile/Georgia_Sotiropoulou
LinkedIn: https://www.linkedin.com/pub/georgia-sotiropoulou/91/887/628

Metrics

Publications: > 85	**Patents: 4**	**GenBank™/PDB: 14**
***h*-index: 38**	**Citations: > 5,000**	**Mean citations per paper: 60**

Education

1987: Ph.D. in Biochemistry, Aristotle University of Thessaloniki, Greece
1980: Diploma in Chemistry, University of Patras, Greece

Professional Appointments and Research Training

2019-now	Professor, Department of Pharmacy, School of Health Sciences University of Patras, Greece
2003-2019	Associate Professor, Department of Pharmacy, University of Patras, Greece
Jan-June 2014	Visiting Professor, *Imagine* Institute INSERM UMR 1163, University Hospital Institute, Université René Descartes Paris 5-Sorbonne Paris Cité, Paris, FRANCE
2015-2020	Affiliated Investigator, Biomedical Research Foundation, Academy of Athens
1993-2003	Assistant Professor, Department of Pharmacy, University of Patras, Greece
1998	Harvard Medical School, Department of Biological Chemistry and Molecular Pharmacology/ Dana-Farber Cancer Institute, Cancer Biology (c/o Prof Arthur Pardee), Boston, MA, USA
1993-1995	Harvard Medical School, Department of Genetics and Microbiology and Dana-Farber
1996 (6 mo)	Cancer Institute, Division of Cancer Genetics (c/o Prof Ruth Sager), Boston, MA, USA
1989-1993	Lecturer, Department of Pharmacy, University of Patras, Greece
1988-1989	Invited Researcher, Institute of Physical & Chemical Research RIKEN, Saitama, JAPAN
1987-1988	Postdoctoral Fellow, NCSR "Demokritos" and Laboratory of Enzymatic Technology, Technological University of Compiegne, Compiègne, FRANCE
1985	Graduate Fellow, Department of Biophysics, University of Osnabrück, GERMANY
1981-1985	Graduate Research Fellow, Institute of Biology, NCSR "Demokritos", Greece

Hellenic Open University

2008-2015	Collaborating Faculty, Master's in Teaching Natural Sciences MSc
2005-2006	Collaborating Faculty, Studies in Natural Sciences

Languages

Greek (mother tongue), English and German (fluent), French and Spanish (basic)

Prizes-Awards

2018 (Athens, Greece) **Empirikion Research Prize**

2014 (NY, USA) **Parkinson's Disease Foundation's International Research Grant Award**

2013 (Toronto, Canada) **"The E. K. Frey - E. Werle Promotion Prize" (2013)**

Awarded by The E. K. Frey - E. Werle Foundation of the Henning L. Voigt Family (Munich, GER).
*For important contributions to contemporary research in the kallikrein-kinin system and related fields***.**

1998 (Boston, USA) **Fulbright Senior Research Award**

Harvard Medical School and the Dana-Farber Cancer Institute

"In vivo and in vitro assays for drug discovery-Functional evaluation of cystatin M as a tumor suppressor by the nude mouse assay. Development of an in vitro assay for screening anticancer drugs using the expression of the green fluorescent protein as a marker.

1998 (Nyborg, Denmark) **American Association for Cancer Research (AACR) Award**-AACR Meeting on "Proteases and Protease Inhibitors in Cancer".

For the original identification and cloning of protease M (KLK6) gene and association to cancer.

1996 (Florida, USA) **American Association for Cancer Research (AACR) Award**-AACR Special Conference on "Proteases and Protease Inhibitors in Cancer Research".

For the original identification and cloning of cystatin M gene and association to cancer.

1993 (Boston, USA) **Fulbright Senior Research Award**

Harvard Medical School and the Dana-Farber Cancer Institute

"*Identification and characterization of molecular markers for cancer Isolation of anti-peptide antibodies based on the identified markers".*

Ranking of Researchers and Scientists in Greece in 2017 (Google Scholar database):

298/7470 upper 3,9%
https://www.scribd.com/document/354081237/Ranking-of-researchers-and-scientists-in-Greece-in-2017-according-to-Google-Scholar-database

Invited Reviewer for Research Grants

Greece	Greek Secretariat of Research & Technology, Ministry of Education, State Scholarships Foundation
Cyprus	Research Promotion Foundation
UK	Breast Cancer Campaign, London
	Worldwide Cancer Research, Scotland
Hungary	The Hungarian Scientific Research Fund, OTKA
Poland	National Science Centre
Austria	The Austrian Federal Ministry of Education, Science and Culture-The Austrian Genome Research Programme GEN-AU
EU	Innovative Medicines Initiative, IMI; www.imi.europa.eu-European Union and the European Federation of Pharmaceutical Industries; Call: "Molecular biomarkers - accelerating cancer therapy development and refining patient care"; invited
Australia	Australian Government Department of Health Funding-Australian Prostate Cancer Research Centre.

Current/Recent Funding

- ERA-NET/E-Rare-3: Joint Translational Call (2015) for "European Research Projects on Rare Diseases".
  Project Title: "Tracing the untackled facets of Peeling Skin Disease-Targeting epidermal proteolysis for treatment" (Propekal5) ["Ιχνηλατώντας τις ανεξερεύνητες πλευρές της νόσου PSD- Στόχευση της επιδερμικής πρωτεόλυσης για θεραπεία"]
  2015-2018, PI: G Sotiropoulou, Total/Partner 1 Budget: €469,197 / €100,000
  Ranked 5th/234 (top 2%)

- Parkinson's Disease Foundation (PDF), International Research Grants Program (IRGP), NY, USA; Project Title: "Novel insights into the properties and fate of naturally secreted alpha-synuclein"
  PDF-IRG-1441; 2014-2016, PI: G Sotiropoulou, Budget: $165,000
  Ranked among 10/210 (top 4.8%)

- 2013 Fondation Santé Grants
  Project Title: "Is KLK6 protease the eluded regulator of extracellular α-synuclein?"
  2013-2015, PI: G Sotiropoulou, Budget: €40,000

- Europa Nostra2014; Greece-France Bilateral Cooperation Project 2013-2015.
  Project Title: "Integration of novel mouse models to advance understanding of epidermal proteolysis in rare genetic skin diseases such as the Netherton Syndrome-Basic and translational aspects".
  2013-2015, ERADISK5, PI: G Sotiropoulou, Budget: €30,000

- Excellence Postdoctoral Grants (LS4-2139, Skink5)
  Project Title: "Delineation of KLK5-mediated proteolytic pathways in skin desquamation"
  2011-2014, PI: G Sotiropoulou, Budget: €150,000

- ΔΡΑΣΗ «ΕΡΕΥΝΩ-ΔΗΜΙΟΥΡΓΩ-ΚΑΙΝΟΤΟΜΩ» (ΕΥΔΕ ΕΤΑΚ-ΕΥΔ ΕΠΑνΕΚ ΕΣΠΑ 2014-2020)
  QFytoTera - Τ1ΕΔΚ-00996
  2018-2021, PI for UPATRAS: G Sotiropoulou, Budget: €100.610
  Project Title: "Nanoemulsions of plant oils with moisturizing and insect repellent properties"
  Τίτλος στα Ελληνικά: "Νανογαλακτώματα φυτικών ελαιών με ενυδατικές και εντομοαπωθητικές ιδιότητες"

- ΔΡΑΣΗ «ΕΡΕΥΝΩ-ΔΗΜΙΟΥΡΓΩ-ΚΑΙΝΟΤΟΜΩ» (ΕΥΔΕ ΕΤΑΚ-ΕΥΔ ΕΠΑνΕΚ ΕΣΠΑ 2014-2020)
  BIOLUMIPD - Τ1ΕΔΚ-03884
  2018-2021, PI for UPATRAS: G Sotiropoulou, Budget: €170.000
  Project Title: "Development of improved biomarker technologies for the discriminative diagnosis of Parkinson disease"
  Τίτλος στα Ελληνικά: "Ανάπτυξη προηγμένης τεχνολογίας βιοδεικτών για την διαφοροδιάγνωση της νόσου Parkinson"

- Ερευνητικά Έργα ΕΛΙΔΕΚ για την Ενίσχυση Μεταδιδακτόρων Ερευνητών/τριών-Θεματική περιοχή: Life Sciences (Medical and Health Sciences), Natural Sciences
  K6PD-1876 (Code: 1876)
  2018-2021, PI: G Pampalakis, Host Lab: UPatraPharmacy/G Sotiropoulou, Budget: €180,000
  Project Title: "α-synuclein prion-like particles: in vivo turnover and infectivity"

Earlier Funding

- Farmaserve-Lilly
  2011, PI: G Sotiropoulou

- Karatheodoris, University of Patras Research Committee
  Project Title: "Evaluation of the role of KLK6 in breast cancer development and/or metastasis in a mouse model and investigation of underlying molecular mechanisms using biotechnology approaches"
  2007-2010, PI: G Sotiropoulou

- PENED2003 (03EΔ430), Greek Secretariat of Research and Technology
  Project Title: "Study of KLK6 function and mechanisms of transcriptional regulation in tumors. Analysis of DNA methylation for the development of molecular diagnostics for cancer. Identification of specific substrates, synthesis and validation of specific and selective inhibitors"
  2006-2008, PI: G Sotiropoulou

- PENED2003 (01EΔ557), Greek Secretariat of Research and Technology
  Project Title: "Development and validation of novel diagnostics for cancer molecular diagnosis and staging"
  2003-2005, PI: G Sotiropoulou

- PENED2003 (01EΔ557), Greek Secretariat of Research and Technology
  Project Title: "Immunomodulation of HER-2 (c-erbB2) oncogene by administration of IFN-γ to improve immunochemotherapy of patients with metastatic breast cancer with Trastuzumab"
  2003-2005, G Sotiropoulou: Collaborating Group Leader

- Research Grant provided by the Mount Sinai Hospital, Toronto, Ontario, CANADA
  Project Title: "Production and biochemical characterisation of recombinant human kallikrein 9 (hK9), human kallikrein 11 (hK11) and human kallikrein 12 (hK12)"
  2002-2003, PI: G Sotiropoulou

- PENED1999, Greek Secretariat of Research and Technology
  2000-2001, G Sotiropoulou: Collaborating Group Leader
  Project Title: "Pathophysiology of bone metastases from hormone-dependent cancers (prostate-breast): Urokinase, protease M and inhibitors of their enzymatic activities"

- NATO Collaborative Research Grant
  Project Title: "Characterization of selected proteases from human normal and tumor cells"
  1998-2001, PI: G Sotiropoulou

- K Karatheodoris, University of Patras Research Committee
  Project Title: "Cloning and analysis of cystatin M promoter and mechanisms of regulation and its inactivation in human breast cancers"
  1998-2001, PI: G Sotiropoulou

- European Association for Cancer Research (EACR)
  2008 Mike Price Fellowship, sponsored by EACR and ECCO–European CanCer Organization
  Project Title: "Molecularly targeted aptamer-based therapeutics and diagnostics directed against specific tumor markers for epithelial cancers"
  Funded the sabbatical visit (for one year) of Assist Prof S Missailidis (Open University UK) in the Department of Pharmacy (c/o G Sotiropoulou)

Professional Affiliations

American Association for Cancer Research (AACR) (1994), Women in Cancer Research (sponsored by the AACR) (1994), International Proteolysis Society (2006), The Kallikrein Society (2005), International Society of Enzymology (ISE) (2010), Association of Fulbright Scholars (1994), Hellenic Society of Biochemistry and Molecular Biology (1984), Association of Hellenic Chemists (1980)

Invited Lectures: > 85

International Meeting Presentations (1994-): >100

Organization of International/National Meetings, Conferences and Workshops: 16

Chair, 5th General Meeting of the International Proteolysis Society (IPS2007)
Conference and Cultural Center, University of Patras, 20-24 October 2007
>530 international participants

Chair:

International Satellite Postgraduate Course on «Proteomics: Methodologies and Applications»
19-20 October 2007, Department of Pharmacy, University of Patras

International Satellite Postgraduate Course on «Bioinformatics-Computational Methods in Biological Data Mining»
19-20 October 2007, Department of Pharmacy, University of Patras

International Satellite Postgraduate Course on «Enzyme Mechanisms and Kinetics»
19-20 October 2007, Department of Pharmacy, University of Patras

International Scientific Committee Member:

The 22nd Congress of the International and European Federations of Clinical Chemistry and Laboratory Medicine of Clinical Chemistry and Laboratory Medicine, IFCC-EFLM EuroMedLab2017; www.athens2017.org
Megaro Mousikis, Athens, Greece, June 11-15, 2017

The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017)
Université F. Rabelais, Tours, France, 26-29 September 2017

8th IEEE International Conference on BioInformatics and BioEngineering (BIBE 2008)
Royal Olympic Hotel, Athens, Greece, October 8-10, 2008

1st International Symposium on Kallikreins (ISK2005)
International Olympic Committee Congress, Lausanne, Switzerland, 1-3 Sept 2005

Organizing Committee Member:

Advances in Circulating Tumor Cells (ACTC2012): From Basic Research to Clinical Practice,
Astir Palace Vouliagmeni – Westin Resort, 26-29 September 2012

4th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2011): Biochemistry, Molecular Biology and Association to Disease
Rhodos Palace Hotel, Rhodes Island, Greece, 2-4 September 2011

7th International Symposium on Minimal Residual Cancer (7th ISMRC Athens 09)
Astir Palace Vouliagmeni, Athens, Greece, September 16-19, 2009

2nd International Symposium on Kallikreins (ISK2007)
Petros M. Nomikos Conference Center, Santorini Island, Greece, 16-18 October 2007

National Meetings, Conferences and Workshops – Member of Organizing Committee

- **Workshop of the Hellenic Proteomics Society**
  Conference and Cultural Center of the University of Patras, 23 May 2006
- **2nd Biosciences Conference**
  Conference and Cultural Center of the University of Patras, 23-24 April 2007
- **57th Annual Meeting of the Hellenic Society of Biochemistry and Molecular Biology**
  Conference and Cultural Center of the University of Patras, December 2006
- **1st Biosciences Conference**
  Conference and Cultural Center of the University of Patras, 19-21 Μαΐου 2005

Invited Reviewer for scientific journals (> 55):

Analytica Chmica Acta | Anti-Cancer Agents in Medicinal Chemistry | BBA - Molecular Cell Research | BBA - Proteins and Proteomics | Biochimie | Biological Chemistry | Biomaterials | Bioorganic and Medicinal Chemistry Letters | BJU International | BMC Cancer | BMC Genomics | British Journal of Dermatology | Cancer | Cancers | Cancer Biomarkers | Cancer Cell International | Cancer Investigation | Clinical Biochemistry | Cell Proliferation | Clinical Chemistry | Clinical Chemistry and Laboratory Medicine | Clinical Proteomics | Comparative Biochemistry and Physiology | Critical Reviews in Clinical Laboratory Sciences | Critical Reviews in Clinical Laboratory Sciences | Current Drug Discovery Technologies | Experimental Dermatology | Expert Review of Molecular Diagnostics | Expert Review of Proteomics | Frontiers in Oncology | Gene | Hypertension Research | International Journal of Biological Sciences | International Journal of Cancer | International Journal of Environmental Research and Public Health | Journal of Pharmacology & Clinical Toxicology | International Journal of Molecular Sciences | Journal of Investigative Dermatology | International Journal of Peptide Research and Therapeutics | Journal of Pharmacology and Clinical Toxicology | Mammalian Genome | Molecular Biology and Evolution | Molecular Biology Reports | Molecular Oncology | Molecular Therapy - Methods & Clinical Development | Natural Product Communications | Nature Structural and Molecular Biology | Novel Biomarkers | Oncogene | Oncotarget | PLoS ONE (editorial board) | Proteins and Peptide Letters (editorial board) | Scientific Reports | The Journal of Pathology | Thrombosis and Haemostasis | Tumor Biology

Administrative Activities

Member of Faculty meeting (Department of Pharmacy, 1989-2018), Member of Faculty Reviewing Committees (1991-2018), Coordinator of Graduate Program in "Pharmaceutical Biotechnology and Biomedical Sciences" (Dept of Pharmacy; 2004-2010), Member of Senate (Syglitos) of the University of Patras (2002-2003), Member of Council of the International Proteolysis Society (IPS, 2005-2007), Member of Council of the International Society of Kallikreins (2004-2015), Member of PhD and MSc theses committees (1990-2015), Alternate member of the Research Committee of the University of Patras (2004), Alternate member of the national committee for narcotics (pharmacology), Academic consultant of DOATAP for Pharmacy and Pharmaceutical Sciences, Committee Member of the Center for Instrumental Analysis, University of Patras (1998-2004), Member of Committee for Graduate and Undergraduate Curriculum, Member of Committee for Academic Development, Member of Committee for Admission Exams in Biochemistry (Department of Pharmacy).

RESEARCH GROUP (2018)

Postdoctoral Researchers

Elini ZINGKOU
Golfo KORDOPATI

PhD Students

Vasia-Samantha SYKIOTIS
Nicolas KHOURY
Evangelos BISSYRIS

MSc Students

Eleni TSIAOUSI
Christina GIANNAKOPOULOU
Kyriaki EVAGELATOU

BSc Students

Maria SARRI
Ozgkiour Antoula CHALIL
Nikos ANTONOPOULOS

Supervisor:

PhD Theses

Vasia-Samantha SYKIOTI (defended 6/2-19)
Eleni ZINGKOU (2018)
Maria KAPASA (2011)
Athanasia PAVLOPOULOU (2011)
Konstantinos DROSOPOULOS (2005)
Georgios PAMPALAKIS (2005)
Eleni DIONYSSOPOULOU (2001)
Eugenia DRAKOPOULOU (1993)

MSc Theses

Helen CHARLA (2017)
Nicolas KHOURY (2015)
Evangelia PROSNIKLI (2012)
Georgios PAMPALAKIS (2002)
Theodoros TSETSENIS (2001)

BSc Theses: > 40

MSc and PhD Committees (UPatras, EKPA): > 30

University Teaching

Department of Pharmacy, University of Patras

Undergraduate Courses:

Pharmaceutical Biotechnology (and Laboratory Training) (2002-2020)

Cell Biology (2004-2020)

Molecular Biology-Genetics (and Laboratory Training) (2005-2010)

Introduction to Biotechnology (1996-2001)

Pharmacognosy I and II (1990-2003)

Diploma Thesis I and II (1996-2018)

Graduate Courses:

Preclinical and Clinical Drug Evaluation (2018-2020)

Molecular Targets of Drug Action (2018-2020)

Applied Biotechnology and Bioinformatics (2018-2020)

Precision Therapeutics (2018-2020)

Pharmaceutical Biotechnology (2002-2018)

Specific Topics in Clinical Chemistry (2011-2013)

Biochemical Basis of Drug Action (1995-2012)

Advanced Biotechnology (2002-2011)

Molecular Diagnostics (2002-2011)

Molecular Biology of Cancer (2002-2011)

Molecular Biology and Biotechnology Techniques (2002-2011)

Bioinformatics and Introduction to Biomedical Research (2002-2011)

Biotechnology Principles (1995-2002)

Pharmaceutical Microbiology (1995-2002)

Natural Products-Pharmacognosy (1995-2002)

Computer Applications in Pharmaceutical Sciences (1995-2002)

Hellenic Open University (http://www.eap.gr)

2008-2015 Collaborating Scientific Stuff (SEP), Master's in Teaching Natural Sciences MSc,
Tutor for postgraduate course: "Organization of Matter in Life Systems"
Module code: KFE53

2005-2006 Collaborating Scientific Stuff (SEP), Studies in Natural Sciences,
Tutor for undergraduate course: "Cell structure and function". Module code: FYE31

Current/Recent Collaborations

1. **Alain Hovnanian,** MD, PhD, Professor and Head
   INSERM UMR S1164 IHU Imagine-Institut des maladies génétiques-Université Paris Descartes, Paris, FRANCE URL: http://www.genegraft.eu/main-investigators
2. **Eleftherios P. Diamandis** MD, PhD, FRCP(C), FRSC, Professor
   Hold'em for Life Chair in Prostate Cancer Biomarkers, Head of Clinical Biochemistry, Mount Sinai Hospital and University Health Network Professor and Head, Division of Clinical Biochemistry, Dept. of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, CANADA
   URL: http://sites.utoronto.ca/acdclab
3. **Kostas Vekrellis**, Researcher B'
   Division of Basic Neurosciences, Biomedical Research Foundation, Academy of Athens, Athens, GREECE URL: http://www.bioacademy.gr/faculty-details/HMw/kostas
   AND Visiting Professor (2011-present)
   University of Oxford, Medical School, Department of Experimental Medicine, Radcliffe Department of Medicine, Oxford, UK
4. **Oliver Schilling,** PhD, Group Leader, ERC Awardee
   Emmy-Noether Research Fellow, Institute for Molecular Medicine and Cell Research, University of Freiburg, Freiburg, GERMANY URL:
   http://www.sgbm.unifreiburg.de/index.php?option=com_zooprofiles&task=userProfile&user=6585
5. **Guy Serre, MD,** PhD, Professor**,** Directeur
   Unité Différenciation Epidermique et Autoimmunité Rhumatoïde (UMR 5165), UDEAR - UMR 5165 CNRS, 1056 INSERM, Université de Toulouse, Hôpital PURPAN, Place du Dr Baylac TSA 40031, Toulouse, FRANCE URL: http://www.udear.cnrs.fr/

   Nathalie Jonca, Professor
   CNRS UMR 5165 - INSERM U1056 - Toulouse III University, CHU Purpan, Place du Dr Baylac - TSA 40031, Toulouse, FRANCE URL: http://www.e2brn.eu/members/jonca.html
6. **Andras Nagy,** Professor and Head and **Dr. Iacovos Michael**
   Department of Molecular Genetics, University of Toronto and Mount Sinai Hospital and Samuel Lunenfeld Research Institute, Toronto, Ontario, CANADA
   URLs: http://www.mshri.on.ca/nagy/
   http://www.phenogenomics.ca/transgenics/links.html and http://www.lunenfeld.ca/researchers/nagy
7. **George M Yousef**, MD, PhD, FRCPC (Path), MSc, MBBCh, Professor
   Department of Laboratory Medicine, St. Michael's Hospital and
   Department of Laboratory Medicine and Pathobiology, University of Toronto, CANADA
   URL: http://www.stmichaelshospital.com/research/profile.php?id=yousef
8. **Dimitra Kiritsi,** Assistant Professor, MD, FEBDV
   Universitaetsklinikum, Klinik für Dermatologie und Venerologie
   University of Freiburg, Freiburg, Germany URL: https://www.uniklinik-freiburg.de/hautklinik/
9. **Evi S. Lianidou,** Professor
   Laboratory of Analytical Chemistry, Analysis of Circulating Tumor Cells (ACTC) Lab, Department of Chemistry, University of Athens, Greece URL: http://en.actc-lab.chem.uoa.gr/
10. **Vassileios Zoumpourlis**, Researcher A'
    Biomedical Applications Unit, Institute of Biological Research and Biotechnology. National Hellenic Research Foundation, Athens, Greece
    URL: http://www.eie.gr/nhrf/institutes/ibrb/serviceunits/bau-en.html

Earlier Collaborations*:*

Ruth Sager, Head at DFCI, Professor, Member of the National Academy of Sciences USA, and the Academy of Sciences and Arts USA
Division of Cancer Genetics, *Dana-Farber Cancer Institute (DFCI), Department of Genetics and Microbiology, Harvard Medical School, Boston, MA, USA*

Arthur B. Pardee, Head at DFCI, Professor, Member of the National Academy of Sciences USA, and the National Academy of Sciences and Arts USA
Division of Cancer Biology, Dana-Farber Cancer Institute, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA, USA

Bonnie F. Sloane, Professor and Chair
Department of Pharmacology, Wayne State Medical School, Detroit, MI, USA

Fransesc X. Aviles, Professor and Chair
Institut de Biologia Fonamental and Departament de Bioquimica Universitat Autonoma de Barcelona, Bellaterra (Barcelona), SPAIN

R. Manjunatha Kini, Professor and Chair
Department of Biological Sciences, Faculty of Science, National University of Singapore, SINGAPORE

Antonia Vlahou, Staff Research Scientist - Professor Level
Proteomics Laboratory, Biomedical Research Foundation, Academy of Athens, Athens, GREECE

Aristotelis Chatziioannou, Researcher B'
Metabolic Engineering–Bioinformatics Programme, Institute of Biological Research and Biotechnology, National Hellenic Research Foundation, GREECE

Vassilis Georgoulias and **Dimitris Mavroudis,** Professors and Head
Laboratory of Tumor Cell Biology, Medical School, University of Crete, GREECE

Invited Lectures (2004-, Selection)

"KLK6 protease is implicated in the regulation of extracellular α-synuclein and may repress its prion-like propagation"
Fondation Santé 2017 Fellows Symposium
Ionic Center, Plaka, Athens, Greece, October 6, 2017

Plenary Speaker: "Role of KLKs in the regulation of immune function"
The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017),
Université F. Rabelais, Tours, France, 26-29 September 2017

"KLK6 proteolysis is implicated in the regulation of extracellular alpha-synuclein species and may represent a novel therapeutic approach"
The International Society for Enzymology Annual Conference: Advances in Laboratory Medicine and Pathobiology 2017 (ISE2017), Santorini Palace, Fira, Thira (Santorini), Greece, June 16-19, 2017

"Rare skin syndromes provide insights and druggable targets for epidermal overdesquamation and inflammation"
"Advances in Laboratory Medicine and Pathobiology 2016" *Under the auspices of the* International Society for Enzymology.
Syros Island, Greece, July 1-4, 2016

"Novel transgenic models reveal druggable targets for skin inflammation"
National and Kapodistrian University of Athens, Chemistry Department, March 3rd, 2016

"Novel animal models for validation of KLK5 protease as a drug target for overdesquamating/inflammatory skin diseases".
1st International CRS Congress, Aegli Zappiou, Athens, Greece, May 27-28, 2015

“Insights into the roles of KLK5 protease in epidermal proteolysis, inflammation and cancer”
UDEAR - UMR 5165 CNRS - U1056, Université Toulouse III, Hôpital Purpan, Toulouse, France, May 6, 2015

"Unravelling the functions of KLK proteases in epidermal inflammation and in Parkinson’s disease. Insights from new animal models"
Pierre et Marie Curie-Sorbonne Universités (UPMC), Paris, France, June 10th, 2014

“Emerging roles of KLK proteases. Insights from new animal models”
Imagine Institute, INSERM UMR 1163, Paris, France, June 25th, 2014

Plenary Speaker: “Insights into KLK functions from novel animal models”
5th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2013) Biochemistry, Molecular Biology, and Association to Disease
St. Michael’s Hospital, Toronto, Ontario, Canada, Sept 28-Oct 1, 2013

"Refining the roles of KLK proteases"
Université Paris 5 René Descartes, Hôpital Necker enfants malades, Paris, France 4th February 2013

"KLK proteases: A road under construction"
Research Seminars Series "Conférence Sézary"
Hôpital St Louis, Paris, France, February 7th, 2013

"Insights into unexpected functions of KLK5/6 proteases"
University of Toronto, Mount Sinai Hospital, Toronto, Ontario, Canada, April 5th, 2012

"The miRNAs in cancer"
19th Postgraduate Conference in Clinical Oncology,
Candia, Heraklion, Crete, Greece, 27-29 October, 2011

"Role of enzymes in human diseases: Human tissue kallikreins: Physiology and clinical applications", New Roles for Old Molecules: Enzymes in Personalized Medicine, International Society for Enzymology
Pilot Beach Resort, Chania, Crete, Greece, 2-4 May 2010

"Emerging roles of human kallikrein-related peptidase 6 in cancer"
6th General Meeting of the International Proteolysis Society (IPS2009)-Workshop on "Kallikreins and other emerging serine proteases in disease"
Surfers Paradise, Gold Coast, QLD, Australia, 26-31 October 2009

"A tumor protective role for KLK6 protease in breast cancer mediated by inhibition of epithelial-to-mesenchymal transition"
7th International Symposium on Minimal Residual Cancer
Astir Palace Vouliagmeni, Greece, 16-19 September 2009

“Emerging roles of human kallikrein-related peptidase 6 in cancer”
6th General Meeting of the International Proteolysis Society
Workshop on “Kallikreins and other emerging serine proteases in disease”
Surfers Paradise QLD, Australia, October 26-31, 2009

"KLK proteolytic cascade pathways in normal physiology and cancer"
3rd International Symposium on Kallikreins and Kallikrein-Related Peptidases;
TUM, Munich, Germany, August 30–September 2, 2009

“A tumour protective role for human kallikrein 6 in breast cancer mediated by inhibition of epithelial-to-mesenchymal transition"
EMBO Workshop on **“**Can epigenetics influence reprogramming and metastatic progression?”
6-9 October 2008, Banz Monastery, Bad Staffelstein, Germany

“Emerging roles of kallikreins in cancer”
“New Molecules in Cancer Therapeutics”
Divany Caravel, Athens, Greece, 12-14 Οκτωβρίου 2007

“The emerging roles of human tissue kallikreins in cancer”
DYAX, Boston, Ma, USA, March 2006

“The emerging roles of human tissue kallikreins in cancer”
National Hellenic Research Foundation, Institute of Biological Research & Biotechnology
SEMINARS 2006, 31 January 2006, Athens, Greece

“Human Kallikrein 6: Mechanisms of Epigenetic Silencing in Breast Tumors **-** A Role in Breast Cancer?”
Workshop on “Functional Genomics of Proteases”
University of Bern, Bern, Switzerland, 20-22 November 2005

“Regulation of Human Kallikrein 6”
1ST International Symposium on Kallikreins
International Olympic Committee Congress Center,
Lausanne, Switzerland, August 31-September 3, 2005

“Αναδυόμενοι ρόλοι των ανθρώπινων καλλικρεϊνών στη μοριακή διάγνωση καρκίνου”
Επιστημονικό Συνέδριο Κέντρου Μοριακής Βιολογίας Νοσοκομείου ΥΓΕΙΑ, 17 Δεκεμβρίου, 2004

“Ταυτοποίηση και μελέτη γονιδίων για την κατανόηση και μοριακή διάγνωση καρκίνου”
1ο Συνέδριο ΒιοΕπιστημών Πανεπιστημίου Πατρών, Πάτρα, 19-20 Μαΐου, 2005

ΆΛΛΕΣ ΔΙΑΛΕΞΕΙΣ

6ο Πανελλήνιο Συνέδριο Φοιτητών Φαρμακευτικής, Αθήνα, Μάϊος 2005
Μεταπτυχιακό Πρόγραμμα Σπουδών Τμήματος Φαρμακευτικής Πανεπιστημίου Πατρών

5ο Πανελλήνιο Συνέδριο Φοιτητών Φαρμακευτικής, Πάτρα, 7-9 Μαΐου 2004
“Φαρμακογονιδιωματική”

Referees

1. **Carlos López-Otín, PhD, Professor, Member of the Royal Academy of Sciences**
   (Real Academia de Ciencias Exactas, Físicas y Naturales)
   "Ramon y Cajal" National Award for Scientific Research 2009

   Chair of Biochemistry and Molecular Biology, University of Oviedo, SPAIN
   Departamento de Bioquimica, Facultad de Medicina
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   del Principado de Asturias (IUOPA)
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2. **Eleftherios P. Diamandis, MD, PhD, FRCP, Professor**
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   Associated Member of the Academy of Athens (Αντεπιστέλλον Μέλος Ακαδημίας Αθηνών)
   Professor and Head, University of Toronto Medical School
   Division of Clinical Biochemistry, Department of Laboratory Medicine and Pathobiology
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3. **Morley D. Hollenberg, DPhi., MD, FRSC, Professor and *ex* Head**

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ONGOING RESEARCH PROJECTS

- SKIN DISEASES: Unraveling the roles of KLK proteases in overdesquamating and inflammatory skin pathologies characterized by a defective epidermal barrier.
  Rare skin syndromes: Proof-of-principle for pharmacological targeting
- PARKINSON DISEASE: Investigating proteolytic pathways for pharmacological targeting
- CANCER: KLK proteases in cancer development and progression
- VENOMICS: Mining snake venoms for novel pharmaceutical proteins
- THERANOSTICS: Development and validation of activity based probes for serine proteases with dual applications as molecular diagnostics & candidate drug compounds (LMW protease inhibitors)

Mouse Models

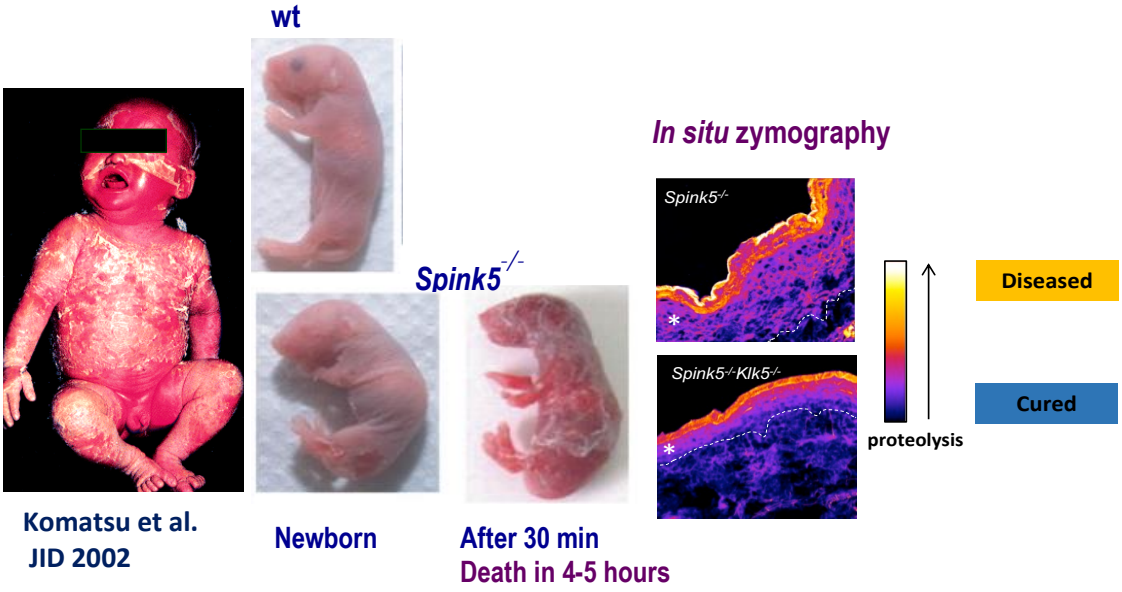
Transgenic / Knockout mouse models (for inflammation and cancer)
Cancer models (breast, skin)

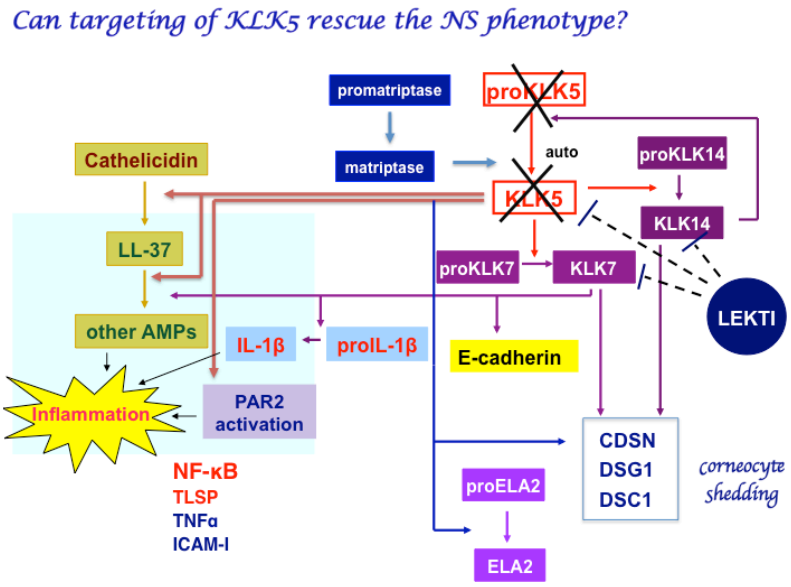
SKIN DISEASES: Unraveling the roles of KLK proteases in overdesquamating and inflammatory skin pathologies characterized by a defective epidermal barrier.
Rare skin syndromes: Proof-of-principle for pharmacological targeting

Our group is interested in the identification and preclinical validation of new drug targets for the therapeutic manipulation of two rare skin diseases: the Netherton syndrome and the Peeling Skin Syndrome-Type B (PSD). Although their genetic basis is distinct, both these diseases are characterized by severe overdesquamation, extensive inflammation, and allergies. Moreover, in both diseases the KLK5 protease is highly activated in the epidermis of patients. Currently, no therapy exists for these devastating diseases, which can be fatal due to the severe skin barrier defect. Studying these rare syndromes will provide proof-of-principle for the design of specific targeted drugs for more common skin diseases, such as atopic dermatitis, rosacea, and psoriasis.

Netherton Syndrome

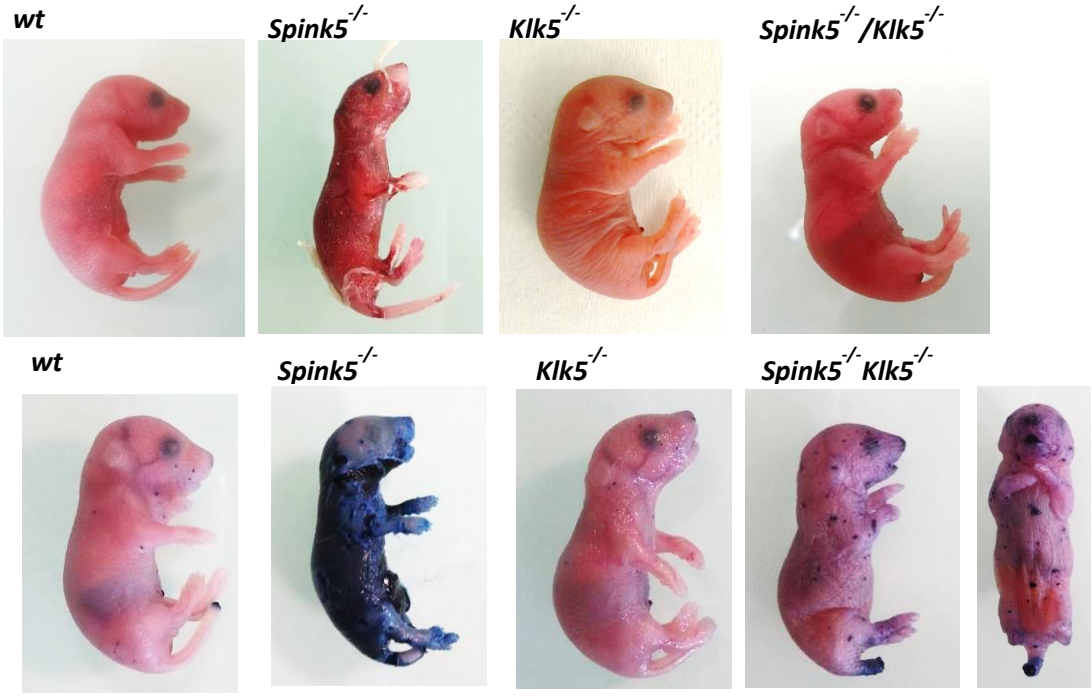
NS is a severe type of ichthyosis, with prevalence 1:200,000 births, and it is caused by inactivating point mutations in the *SPINK5* gene encoding the LEKTI inhibitor of KLKs and other serine proteases. LEKTI deficiency results in hyperactivation of KLK proteases in the epidermis. These unopposed proteolytic activities lead to premature dissociation of the stratum corneum at the junction with the stratum granulosum. The phenotype is severe desquamation and inflammation that often leads to neonatal death due to dehydration. The syndrome is recapitulated in *Spink5*$^{-/-}$ mice that are born normal and die quickly within <5 h from birth. Using novel mouse models, such as *Klk5*$^{-/-}$ mice and *Spink5*$^{-/-}$*Klk5*$^{-/-}$ double knockout mice, our group in collaboration with the group of Professor Alain Hovnanian (*Imagine* Institute, INSERM, Necker Hopital, Paris, France) demonstrated recently that KLK5 is a key molecule for pharmacological inhibition in order to reverse the cutaneous hallmarks of NS (PLoS Genetics Sept 2015). http://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1005389





Proposed proteolytic cascade implicated in skin desquamation and inflammation.

In normal skin, KLK serine proteases in the stratum corneum (SC) act to degrade the intercellular adhesion proteins DSG1, DSC1, and CDSN leading to corneocyte shedding (desquamation) and skin renewal. LEKTI encompasses 15 domains and the corresponding peptides (generated proteolytically) inhibit different serine protease activities in the epidermis. A finely tuned balance of proteases and LEKTI ensures physiological skin desquamation. In NS patients, genetic defects in *SPINK5* lead to the production of a truncated LEKTI precursor protein containing fewer/or no functional inhibitor domains resulting in highly elevated proteolytic activities in the SC, excessive degradation of desmosomal adhesion proteins leading to overdesquamation and a severe skin barrier defect associated with sustained/constitutive epidermal inflammation and atopy.

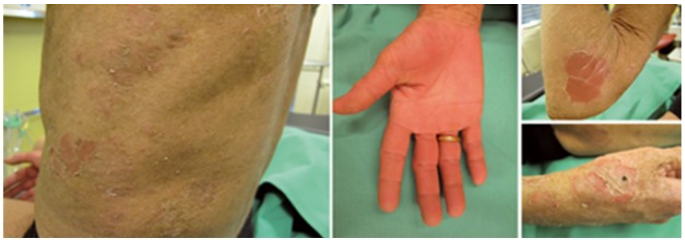


Ablation of *Klk5* rescues skin and whisker anomalies and restores epidermal function in the Lekti-deficient background (*Spink5*$^{-/-}$). The severe skin barrier defect is reversed in *Spink5*$^{-/-}$*Klk5*$^{-/-}$ mice as demonstrated by impermeability of the toluidine blue dye in sharp contrast to the deep blue stain of *Spink5*$^{-/-}$ mice. Photos were taken 30 hours after birth and 5 hours for *Spink5*$^{-/-}$.

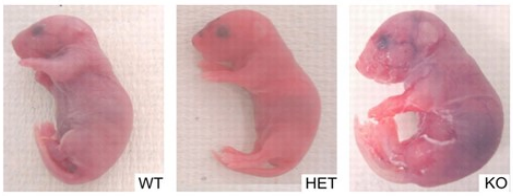
Furio L, Pampalakis G, Michael IP, Nagy A, Sotiropoulou G*, Hovnanian A.* (2015) Elimination of KLK5 reverses the hallmarks of Netherton syndrome. PLoS Genet 11(9):e1005389

Peeling Skin Disease or Peeling Skin Syndrome-Type B

PSD has a similar phenotype with NS but it is caused by mutations in the *CDSN* gene encoding for the corneodesmosin. CDSN is either required for the formation of mechanically resistant corneodesmosomes that hold together the corneocytes of the stratum corneum or its role is to protect desmosomes from premature proteolysis. It is a very rare disease with 30 cases reported worldwide.
Recently funded by the ERA-NET/E-Rare-3 program we will investigate whether targeted inhibition of the KLK5 protease is sufficient to fully or partially alleviate the symptoms of the disease and to examine the molecular pathways associated with PSD.



Mallet et al. (2013) Br J Dermatol 169: 1322-1325.



Leclerc et al. (2009) J Cell Sci 122: 2699-2709.

Funding

PSS type B

- ✓ ERA-NET/E-Rare-3: Joint Translational Call (2015) for "European Research Projects on Rare Diseases".

  Project Title: "Tracing the untackled facets of Peeling Skin Disease-Targeting epidermal proteolysis for treatment" (Propekal5) [2015-2018]

  Coordinator (PI): Georgia Sotiropoulou
  Partners: Nathalie Jonca (University of Toulouse III and Hôpital Purpan, Toulouse, France) and Oliver Schilling (Institute of Molecular Medicine and Cell Research, University of Freiburg, Freiburg, Germany).

Netherton

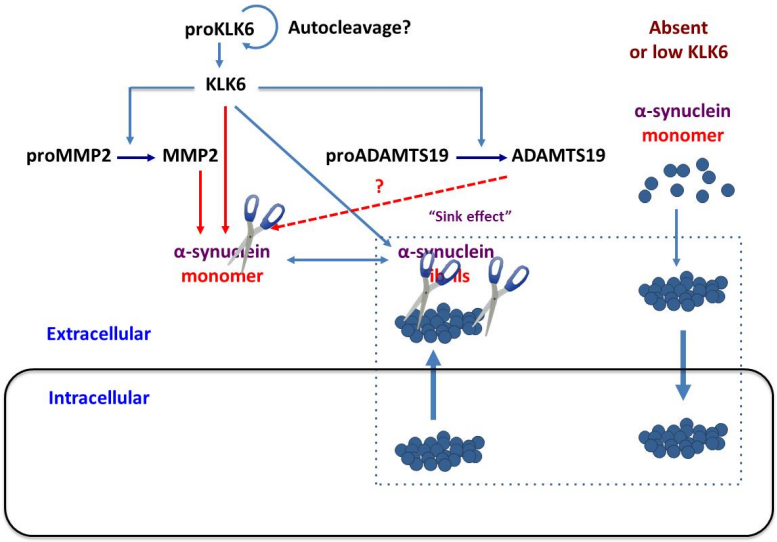
- ✓ Europa Nostra2014; Greece-France Bilateral Cooperation Project 2013-2015.
  Project Title: "Integration of novel mouse models to advance understanding of epidermal proteolysis in rare genetic skin diseases such as the Netherton Syndrome-Basic and translational aspects" [ERADISK5, 2013-2015, PI: Georgia Sotiropoulou]
- ✓ Excellence Postdoctoral Grants (LS4-2139, Skink5)
  Project Title: "Delineation of KLK5-mediated proteolytic pathways in skin desquamation"
  [2011-2014, PI: Georgia Sotiropoulou]

Patent

Hovnanian A, Sotiropoulou G, Pampalakis G, Furio L. (2014) "Methods and pharmaceutical compositions for the treatment of Netherton syndrome". Application Nr: EP14153629.2 Priority date: 2014-02-03; Filing date: 2015-02-02; Publication date: 2015-08-06, WO2015114144A1
https://patents.google.com/patent/WO2015114144A1/en?q=klk5&q=inhibitors

PARKINSON DISEASE: Investigating proteolytic pathways for pharmacological targeting

A hallmark of Parkinson Disease (PD) is the presence in the brain of intracellular inclusions of α-synuclein protein termed Lewy bodies or Lewy neuritis. Alpha-synuclein was thought to be an intracellular protein until recently when it was demonstrated that α-synuclein is also a secreted protein and, importantly, can spread from cell-to-cell in a prion-like mechanism. Nonetheless, the mechanisms that regulate the turnover of extracellular α-synuclein are unknown. In collaboration with Kostas Vekrellis' Group at the Biomedical Research Foundation of the Academy of Athens, we suggested that kallikrein-related peptidase 6 (KLK6) mediates the degradation of extracellular α-synuclein directly and *via* a proteolytic cascade that involves metalloprotease(s). We also found that association of naturally secreted α-synuclein with lipids renders it resistant to proteolysis (Ximerakis M et al. FASEB J 2014). These findings provided the first evidence that physiological modifications affect the biochemical behavior of secreted α-synuclein and that a proteolytic activation cascade may be involved in its catabolism, thus, providing novel insights into mechanisms and potential targets for therapeutic intervention. It should be noted that KLK6 is a serine protease highly expressed in the nervous system, while in synucleinopathies, including Parkinson disease, the levels of KLK6 inversely correlate with α-synuclein in CSF. By degradomic profiling we analyzed the repertoire of proteases activated by KLK6 in a neuronal environment and found that KLK6 activates the proMMP2 and ADAMTS19, which in turn can cleave the α-synuclein. Importantly, we showed that recombinant and naturally secreted KLK6 can readily cleave α-synuclein fibrils that have the ability for cell-to-cell propagation. Using our recently generated *Klk6* knockout mice and established transgenic models for PD, we study the roles of KLK6 in the turnover of extracellular α-synuclein and α-synuclein fibrils and their propagation *in vivo*. It appears that KLK6-deficient primary cortical neurons have increased ability for α-synuclein fibril uptake. By use of new adenoviral vectors for KLK6 delivery we demonstrate that the levels of extracellular α-synuclein can be regulated by neuronally secreted KLK6 (Pampalakis et al. Oncotarget 2016). Our findings open up the possibility to exploit KLK6 as a novel therapeutic target for Parkinson disease and other synucleinopathies.



Schematic representation of the proposed proteolytic cascade leading to proteolysis of α-synuclein monomers and fibrillar strains (Pampalakis et al. Oncotarget 2016)

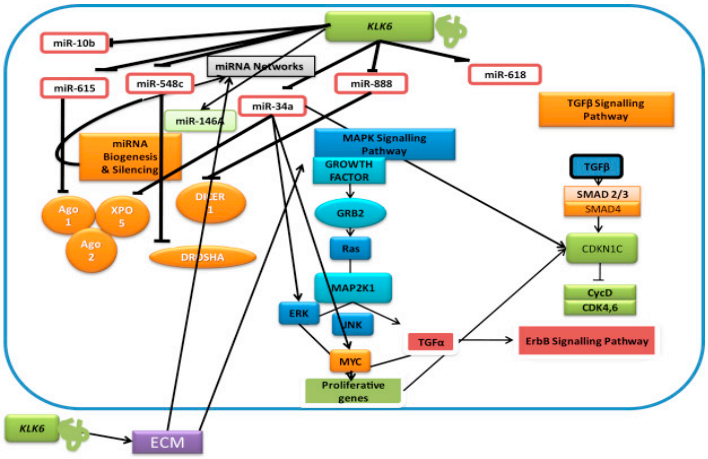
Funding:

- ✓ Parkinson's Disease Foundation (PDF), International Research Grants Program (IRGP), NY, USA; Project Title: "Novel insights into the properties and fate of naturally secreted alpha-synuclein" [2014-2016]
- ✓ 2013 Fondation Santé Grants: "Is KLK6 protease the eluded regulator of extracellular α-synuclein?" [2013-2015]

CANCER: KLK proteases in cancer development and progression

Selection of recent studies:

Sidiropoulos KG, Ding Q, Pampalakis G, White NMA, Boulos P, Sotiropoulou G*, Yousef GM* (2016) KLK6-regulated miRNA networks activate oncogenic pathways in breast cancer subtypes. Mol Oncol 10: 993-1007. https://www.ncbi.nlm.nih.gov/pubmed/27093921



A proposed model for the prediction of KLK6-miRNA interactions

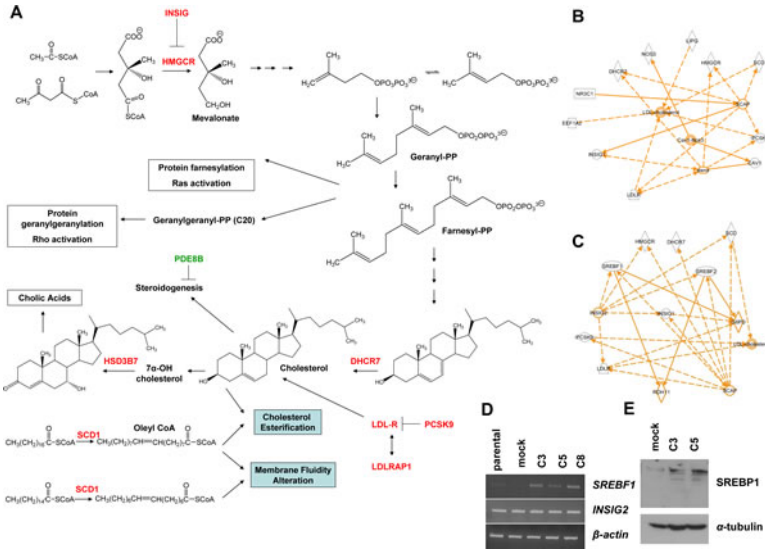
Sidiropoulos et al. Molecular Oncology 2016

Sidiropoulos KG, White NMA, Bui A, Ding Q, Boulos P, Pampalakis G, Khella H, Samuel JN, Sotiropoulou G, Yousef GM. (2014) Kallikrein-related peptidase 5 induces miRNA-mediated anti-oncogenic pathways in breast cancer. Oncoscience 1: 709-724.
https://www.ncbi.nlm.nih.gov/pubmed/25593998

Pampalakis G, Politi AL, Papanastasiou A, Sotiropoulou G. (2015) Distinct cholesterogenic and lipidogenic gene expression patterns in ovarian cancer-A new pool of biomarkers. Genes Cancer 6: 472-479. https://www.ncbi.nlm.nih.gov/pubmed/26807200

Pampalakis G, Obasuyi O, Papadodima O, Chatziioannou A, Zoumpourlis V, Sotiropoulou G. (2014) The KLK5 protease suppresses breast cancer by repressing the mevalonate pathway. Oncotarget 15: 2390-2403. http://www.ncbi.nlm.nih.gov/pubmed/24158494

Pampalakis G, Prosnikli E, Agalioti T, Vlahou A, Zoumpourlis V, Sotiropoulou G. (2009) A tumor-protective role for human kallikrein-related peptidase 6 in breast cancer mediated by inhibition of epithelial-to-mesenchymal transition. Cancer Res 69: 3779-3787.
http://www.pharmacy.upatras.gr/media/GSotLub/1_CancerRes2009withSupplData.pdf

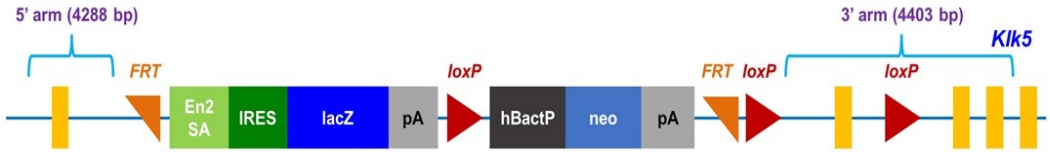


Pampalakis et al. Oncotarget 2014

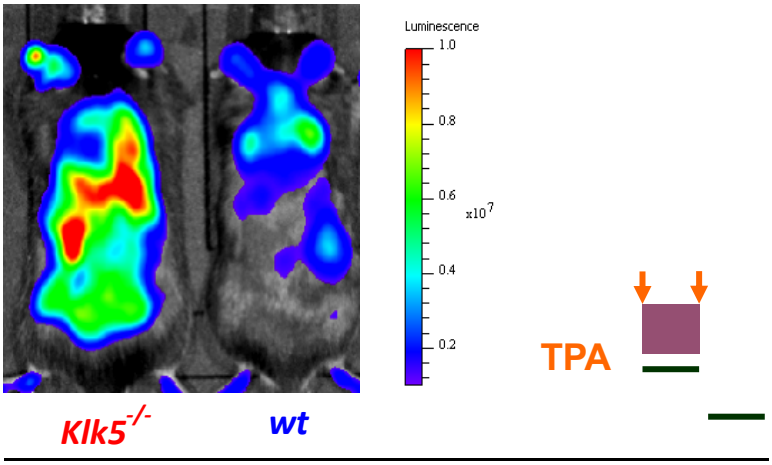
MOUSE MODELS

Transgenic / Knockout Mouse Models (for Inflammation and Cancer)

Recently, we generated transgenic mice that carry a targeted deletion of either the Klk5 or the Klk6 protease, in collaboration with Dr. Iacovos Michael and Prof Andras Nagy (University of Toronto, Canada). The scheme below shows the targeting cassette used for the generation of *Klk5*$^{-/-}$ mice, which allows for a global or a conditional knockout.



In addition, we have generated a novel transgenic/knockout mouse (NGL *Klk5*$^{-/-}$) to monitor Nf-κB activation *in vivo* in the whole animal (shown in the figure below). In transgenic *Ngl* mice a reporter luciferase gene is integrated. The Nf-κb reporter is under the control of a minimal promoter carrying eight Nf-κb consensus sequences upstream of the firefly luciferase gene. Skin inflammation is induced by TPA according to established protocols and Nf-κb activity is monitored with IVIS bioluminescence imaging under anesthesia.



Cancer models

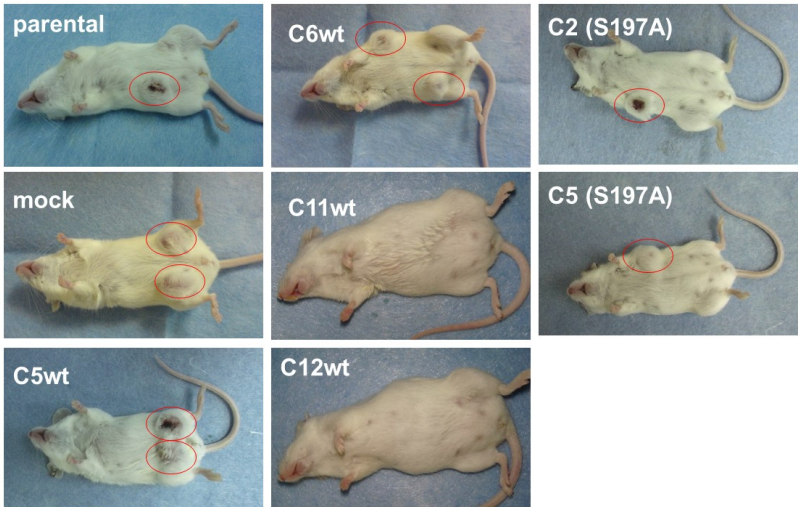
1. Tumor xenografts in immunocompromised mice

Our group uses SCID mice to study cancer growth and dissemination. Cancer cells (either parental or genetically modified by specific gene transfer) are xenotransplanted orthotopically onto SCID mice and primary tumor formation is monitored for several weeks depending on tumor growth rates. At the end of the experiment, mice are euthanized and tumor progression to metastatic sites in vital organs (lung, liver, brain, bone) is recorded. Tumors and their normal adjacent tissues are resected for histological observation by E/H staining and immunohistochemistry. We employed such models to elucidate the role(s) of KLK5 and KLK6 in human breast cancer. A typical experiment is shown in the figure on next page.

Relevant References

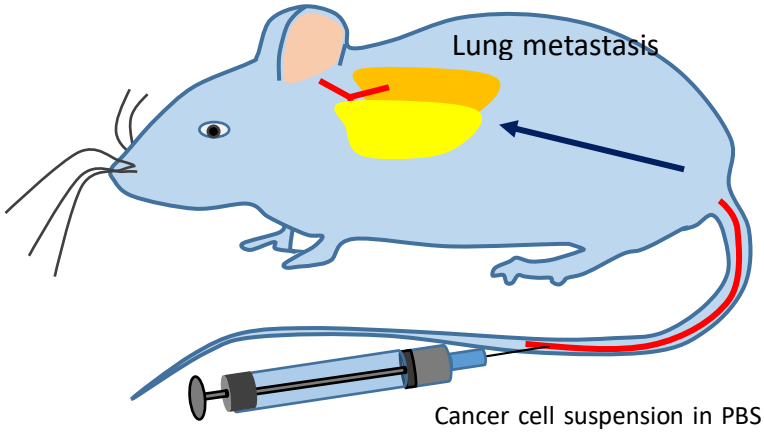
Pampalakis G, Obasuyi O, Papadodima O, Chatziioannou A, Zoumpourlis V, Sotiropoulou G (2014) The KLK5 protease suppresses breast cancer by repressing the mevalonate pathway. Oncotarget 15: 2390-2403. http://www.ncbi.nlm.nih.gov/pubmed/24158494

Pampalakis G, Prosnikli E, Agalioti T, Vlahou A, Zoumpourlis V, Sotiropoulou G (2009) A tumor-protective role for human kallikrein-related peptidase 6 in breast cancer mediated by inhibition of epithelial-to-mesenchymal transition. Cancer Res 69: 3779-3787.
http://www.pharmacy.upatras.gr/media/GSotLub/1_CancerRes2009withSupplData.pdf



2. Tumor Metastasis Assay - Tail Vein Assay

Metastatic breast cancer cell lines (*e.g.* MDA-MB-231, MDA-MB-468) are injected *via* the mice tail vein, as shown in the figure below. Eight weeks post-injection visible tumors are present in the lungs (and other vital organs) of the injected mice, which are excised, quantified, and biopsied to assess metastatic disease.

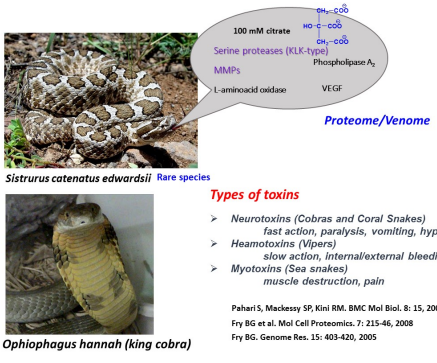


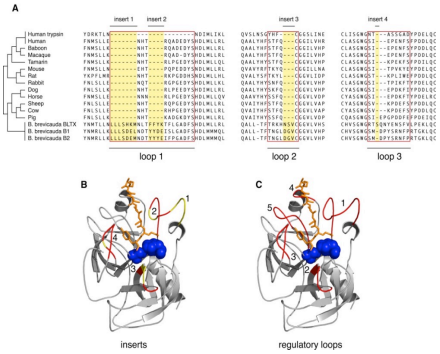
3. Chemical carcinogenesis in transgenic mice

We use knockout models to delineate the role of proteases in cancer development. To investigate the possible role(s) of KLK5 and KLK6 proteases in skin cancer we employ chemical carcinogenesis in *Klk5*$^{-/-}$ and in *Klk6*$^{-/-}$ mice. Skin tumors are induced by two different schemes: DMBA/TPA and DMBA/DMBA. Our goal is to find new KLK-mediated pathways that are associated with the different stages of tumorigenesis, *i.e.* initiation, promotion, and metastatic progression. Since chemical carcinogenesis in mice is an inflammation-driven process it is expected to reveal the inflammatory mechanisms implicated in skin cancer. In this direction we also apply two well-establish systems of chemical-induced inflammation, *i.e.* the irritant and the allergic contact dermatitis, in order to further elucidate the role of KLKs in skin inflammation. Finally, we also employ the model of methylcholanthrene-induced firbosarcomas to delineate the role of KLKs in this type of cancer.

VENOMICS: Mining snake venoms for novel pharmaceutical proteins

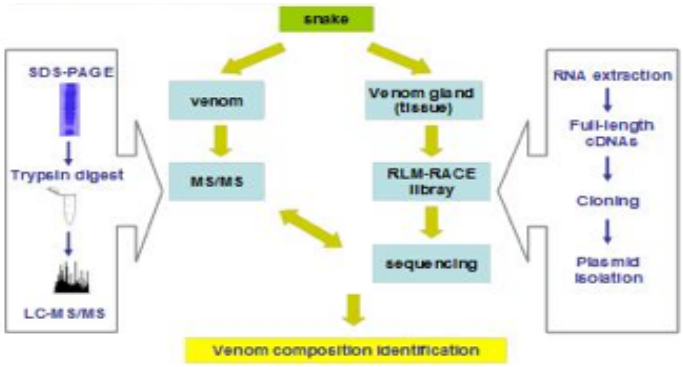
Venomous snakes are "living Pharmacies" unexploited to the largest extent. They are regarded as “oceans of opportunity” for the identification of novel bioactive molecules. Relative to other organisms, snake venoms evolve at greatly accelerated rates, thus, they present remarkable variety. Widely prescribed drugs - as for example the captopril for the treatment of hypertension and some types of congestive heart failure - were discovered from knowledge of venom toxins. To identify novel toxins, we analyse the transcriptome of the venom gland by generating full-length cDNA libraries and sequencing of clones. By integrated HTP proteomics (venomics) and bioinformatics approaches we analyse the complete venom proteome ("venome", *i.e.* the peptides/proteins present in the venom). Our interest in these studies originates in the fact that among the small number (~100-200) of proteins in snake venoms are toxins (SV-Klks, Snake Venom Klks), which display sequence homology to human KLK proteases. We use *c*DNA libraries from the viper snake *Sistrurus catenatus* (provided by Prof RM Kini, University of Singapore).





In particular, our group is interested in the identification of the repertoire of toxins present in the venom of *Vipera ammodytes meridionalis*, the viper snake indigenous in Greece that is responsible for the highest number and most serious and life-threatening envenomations.

Vipera ammodytes is indigenous venomous snake that was collected near Patras Univ. The venom gland transcriptome and venome (venom proteome) are integrated to identify and isolate novel toxins, “leads” for drug discovery and development.



Why studying the venome?

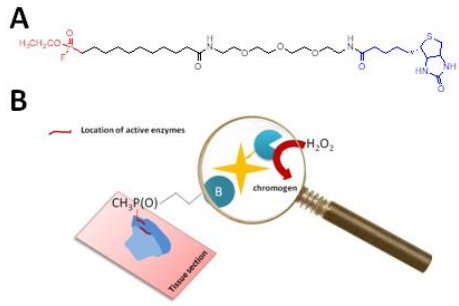
1. **To discover new specific anti-venom therapies.**

Current therapies rely on administration of antivenoms generated by immunizing large animals, which involve risk of allergic reactions, and different venom constituents exhibit variant immunogenicity. Anti-venoms contain numerous antibodies against weak or non-toxin components that dilute their effectiveness. As a result, large antivenom volumes are used further increasing the probability of adverse effects.

2. To identify novel Klk-like toxins.

Remarkably, small amino acid substitutions in enzymes found in venom result in enhanced catalytic activities compared to their ancestor physiological enzymes, to potentiate their lethal function. In the top right figure (adapted from Aminetzach et al. Curr Biol 19: 1925-1931, 2009), sequence and 3D structure comparisons revealed specific insertions or deletions in the mammalian blarina toxin, conferring structural alterations that often render venom toxins unusually active enzymes. It is expected that analogous substitutions have occurred in snake venom toxins. We seek to isolate novel SV-Klks (namely serine proteases with homology to human KLKs but with enhanced enzymatic activity) and to characterize their enzymatic activity and structure with the aim to identify structural features associated with enhanced KLK protease activity. The ultimate purpose is to produce recombinant toxins of pharmacological interest and to aid the design/optimization of potent KLK inhibitors.

THERANOSTICS: Development and validation of activity based probes for serine proteases for dual applications as molecular diagnostics and candidate drug compounds (LMW protease inhibitors)
Often drugs fail at late stages of development because, although the drug target is indeed overexpressed in a disease state, it could occur in the inactive form due to inefficient activation or inactivation by inhibitors. Classical proteomic and gene expression approaches can identify overexpressed proteins/enzymes but fail to identify their "in situ" (at the site targeted by the drug) enzymatic activities implicated in pathology. Proteases, in particular, are popular drug targets in multiple disorders (cancer, neurodegeneration, skin diseases, cardiovascular diseases *etc*) with many examples of widely used marketed drugs targeting proteases (Drag and Salvesen Nat Rev Drug Discov 9: 690-701, 2010; Turk B. Nat Rev Drug Discov 5:785-799, 2006; Sotiropoulou and Pampalakis Trends Pharmacol Sci 33: 623-634, 2012). For the last 20 years, we have extensively studied and contributed to the delineation of the role of the group of serine proteases named kallikrein-related peptidases, in breast cancer, in skin disorders associated with aberrant desquamation and inflammation, and in Parkinson's Disease. It is known that proteases are regulated at multiple from gene expression to posttranslational modification (*i.e.* production of inactive zymogens, internal cleavage and in-/de-activation, inactivation by complex formation with their endogenous inhibitors). Thus, the fraction of the active protease molecules in certain (patho)physiological states remains elusive. We have developed specific activity-based probes (APBs) as tools for *in vitro* and *in vivo* labeling of active enzymes. For proof-of-concept we have focused on selected serine proteases (KLKs) and their activity mapping in skin disorders. We have designed and chemically synthesized ABPs with specificity for the KLK enzymes, which accommodate dual properties in the same scaffold so that they can be used: [1] as molecular diagnostics (activity reporters) and [2] as inhibitors representing potential therapeutics (theranostics). These new ABP molecules are characterized *in vitro*, used to develop new diagnostic assays, and validated for their effectiveness in protease targeting and their theranostic action in novel preclinical mouse models for skin inflammatory diseases that we have generated and characterized.



A, The structure of an organophosphonofluoridate ABP (B24P) synthesized by us. Red color shows the reactive group, black the spacer and blue the biotin detection tag (Pampalakis et al. Chem Commun 53:3246-3248, 2017). B, Schematic diagram of the activography. Briefly, biopsy cryosections are allowed to react with B24P and the overall serine protease activities are quantified with streptavidin-peroxidase chromogenic reaction.

ABPs are small organic molecules used to map various enzymatic activities (serine proteases, oxidases *etc*) in a process known as ABP profiling (ABPP). They bind to enzymes with a covalent bond formed between an electrophile on the ABP and the active-site nucleophile of the enzyme such as the catalytic serine for serine proteases (Sanman and Bogyo, Annu Rev Biochem 83:249-273, 2014). Thus, only catalytically competent proteases bind to ABP irreversibly. The ABPs consist of three parts, a reactive functional group (recognition group), a spacer and a reporter tag. Figure 1A shows the structure of an ABP we recently synthesized. The reporter is used for the detection and is adaptable to various analytical platforms (fluorescence, mass spectrometry, chromogenic reactions, *in vivo* imaging *etc*). The **great advantage of ABPs is that they report on changes in enzymatic activities, rather than total protein or mRNA abundance**. The development of ABPs is a rapidly evolving field, since they offer **unique advantages in the identification/validation of novel pharmacological targets but also in molecular diagnosis**. ABPs can be used for *in vivo* imaging of enzyme activities (Speers et al. J Am Chem Soc 125: 4686-4687, 2003; Edgington and Bogyo, Curr Protoc Chem Biol 5: 25-44, 2013). A **revolutionizing application of ABPs is their use in oncological surgery** to map the tumor margins for complete dissection and to localize remaining tumor microfoci (Cutter et al. PLoS One 7:e33060, 2012). Finally, **ABPs can be easily commercialized** not only for therapeutic/diagnostic applications but also as research tools as demonstrated by the prototype ABP developed by Liu et al. (PNAS 96: 14694-14699, 1999) to target serine hydrolases, commercialized by Santa Cruz Biotechnology (https://www.scbt.com/scbt/product/ fp-biotin-259270-28-5) as a new research reagent to identify active enzymes that react with organophosphates or active serine hydrolases.

LIST OF PUBLICATIONS

Patents

1. **Sotiropoulou G**, Pampalakis G, Bissyris E. (2018) “Theranostic inhibitors and activity-based probes for the KLK7 protease” Patent Application Nr: 2018010052/16/11/2018.
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88. **Sotiropoulou G**, Papageorgiou GC. (1985) Modulation of the Hill reaction rates by ions interacting with the outer surface of cyanobacterial thylakoids. In: Ion Interactions in Energy Transfer Biomembranes (Papageorgiou GC, Barber J, Papa S, eds), 303-312, Plenum Press, New York.

89. Papageorgiou GC, Kalosaka K, Lagoyanni T, **Sotiropoulou G.** (1985) The role of cations in the photoinduced electron transport of cyanobacteria. Recent Advances in Biological Membrane Studies: Structure and Biogenesis, Oxidation and Energetics (Packer L, ed), 369-391, Academic Press, New York.

90. **Sotiropoulou G**, Lagoyanni T, Papageorgiou GC. (1984) Effects of Ca^{2+} ions on the light-induced electron transport activities of Anacystis nidulans permeaplasts and spheroplasts. Adv Photosynth Res 2: 663-666.

ORIGINAL SEQUENCE SUBMISSIONS [GenBank™/EMBL]

National Center for Biotechnology Information: http://www.ncbi.nlm.nih.gov

GenBank™/EMBL: 11 (U62800, U62801, U14550, AY318867, AY318868, AY318869, AY318870, AY457039, AF079516, AY804248, DQ223012)

PDB : 1 (1GVL)

1. DQ641251: Homo sapiens new PSA transcript variant, mRNA, partial cds
   1221 bp mRNA linear (Direct Submission: 16-MAY-2006)
   Pampalakis G, **Sotiropoulou G.** Identification of new PSA isoform.

2. DQ223012: Homo sapiens kallikrein 6 precursor (KLK6)
   (Direct Submission: 26-SEP-2005) mRNA, complete cds, alternatively transcript variant 3. LOCUS: DQ223012, 842 bp mRNA linear
   Pampalakis G, **Sotiropoulou G.** Identification of a novel KLK6 transcript variant

3. AY804248: Homo sapiens kallikrein 6 (KLK6) gene, 5' flanking region
   LOCUS: AY804248, 319 bp DNA linear
   Sotiropoulou G, Pampalakis G. (Direct Submission: 27-OCT-2004)

4. AY457039: Homo sapiens kallikrein 6-like mRNA, complete cds
   Pampalakis G, Sotiropoulou G. Cloning of novel transcript variants of human kallikrein 6/protease M/zyme/neurosin gene (KLK6)

5. AY318867: Homo sapiens kallikrein 6 precursor (KLK6) mRNA, complete cds
   LOCUS: AY318867, 1517 bp mRNA linear (Direct Submission: 09-JUN-2003)
   Pampalakis G, Diamandis EP, **Sotiropoulou G.** Cloning of novel transcript variants of the human kallikrein 6/protease M/zyme/neurosin gene (KLK6)

6. AY318868: Homo sapiens kallikrein 6-like mRNA, complete sequence
   LOCUS: AY318868, 820 bp mRNA linear (Direct Submission: 10-JUN-2003)
   Pampalakis G, Diamandis EP, **Sotiropoulou G.** Cloning of novel transcript variants of the human kallikrein 6/protease M/zyme/neurosin gene (KLK6)

7. AY318869: Homo sapiens kallikrein 6 precursor (KLK6) mRNA, complete cds
   LOCUS: AY318869, 1503 bp mRNA linear (Direct Submission: 09-JUN-2003)
   Pampalakis G, Diamandis EP, **Sotiropoulou G.** Cloning of novel transcript variants of the human kallikrein 6/protease M/zyme/neurosin gene (KLK6)

8. AY318870: Homo sapiens kallikrein 6-like mRNA, complete sequence
   LOCUS: AY318870, 929 bp mRNA linear (Direct Submission: 10-JUN-2003)
   Pampalakis G, Diamandis EP, **Sotiropoulou G.** Cloning of novel transcript variants of the human kallikrein 6/protease M/zyme/neurosin gene (KLK6)

9. NM002774: Homo sapiens kallikrein 6 (neurosin, zyme) (KLK6), mRNA

LOCUS: NM002774, 1512 bp, mRNA linear
Gomis-Ruth FX, Bayes A, **Sotiropoulou G**, Pampalakis G, Tsetsenis T, Villegas V, Aviles FX, Coll M. (2002)

10. U14550: Human sialyltransferase SThM (*sthm*) mRNA, complete cds.
    Locus: HSU14550, 1908 bp, mRNA (Direct Submission: 07-NOV-1994)
    Sotiropoulou G, Anisowicz A, Sager R. (1994) Isolation and cloning from human mammary epithelial cells of a complete cDNA sequence homologous to other known sialyltransferases.

11. U62800: Homo sapiens cystatin M (CST6) mRNA, complete cds
    Locus: HSU6280, 577 bp mRNA
    Sotiropoulou G, Anisowicz A, Sager R. (Direct Submission: 02-JUL-1996)

12. U62801: Human Protease M mRNA, complete cds
    Locus: HSU62801, 1506 bp mRNA
    Anisowicz A, **Sotiropoulou G**, Sager R. (Direct Submission: 02-JUL-1996)

13. AF079516: Homo sapiens small proline-rich protein 1 (SPR1), promoter region.
    Locus: AF079516, 634 bp DNA
    Anisowicz A, **Sotiropoulou G**, Sager R. (Direct Submission: 21-JUL-1998)

PDB Database

14.1GVL_A Chain A, Human Prokallikrein 6 (hK6) Prozyme Proprotease M Proneurosin
LOCUS: 1GVL_A, 223 aa PDB: molecule 1GVL (Method: X-ray Diffraction)
Gomis-Ruth FX, Bayés A, **Sotiropoulou G**, Pampalakis G, Tsetsenis T, Vigellas V, Avilés FX, Coll M. (Direct Submission: 14-Feb-2002)

SELECTED PRESENTATIONS IN INTERNATIONAL SCIENTIFIC CONFERENCES (1994-selected)

1. Nauroy P, Zingkou E, Athanasiou I, Dengjel J, Sotiropoulou G, Nystrӧm A, Kiritsi D. (2020) Kallikrein 6, an epidermally secreted protease, contributes to inflammation and fibrosis during Recessive Dystrophic Epidermolysis Bullosa disease progression. *Matrix Biology Europe Congress 2020 (MBE2020)*, Florence, Italy, 24-28 May 2020
2. Kordopati GG, Zingkou E, Angelis G, Stefanis I, Karioti A, Bilia A-R, Tsiftsoglou O, Chafouz R, Lazari D, Vekrellis K, Magriotis P, Sotiropoulou G, Pampalakis G. (2020) Identification of new phytochemicals that inhibit α-synuclein fibrilization to prevent or delay the progression of Parkinson disease. *20th International Congress of the International Society for Ethnopharmacology*, 27-29 April 2020, Capsis Hotel, Thessaloniki, Greece
3. Pampalakis G, Sykioti V-S, Ximerakis M, Melki R, Vekrellis K, Sotiropoulou G. (2017) KLK6 represses alpha-synuclein prion-like propagation with potential pharmacological applications. *The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017)*, Université F. Rabelais, Tours, France, 26-29 September 2017
4. Sotiropoulou G. (2017) Role of KLKs in the regulation of immune function. *The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017)*, Université F. Rabelais, Tours, France, 26-29 September 2017
5. Pampalakis G, Zingkou E, Valari M, Kiritsi D, Jonca N, Sotiropoulou G. (2017) Activography: A novel, versatile and easily adaptable histochemical method for monitoring enzymatic activities. Validation in biopsy specimens. *The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017)*, Université F. Rabelais, Tours, France, 26-29 September 2017
6. Zingkou E, Pampalakis G, Sotiropoulou G. (2017) Effective therapy for Netherton syndrome requires combined targeting of KLK5 and TNFα. *The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017)*, Université F. Rabelais, Tours, France, 26-29 September 2017
7. Pampalakis G, Zingkou E, Charla E, Jonca N, Schilling O, Sotiropoulou G. (2017) Delineation of the role of the KLK5 protease in Peeling Skin Disease. *The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017)*, Université F. Rabelais, Tours, France, 26-29 September 2017
8. Zingkou E, Pampalakis G, Charla E, Sotiropoulou G. (2017) The double knockout mouse *Spink5-/- Klk6-/-* reveals that *KLK6* is implicated in skin inflammation. *The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017)*, Université F. Rabelais, Tours, France, 26-29 September 2017
9. Khoury N, Pampalakis G, Zingkou E, Zoumpourlis V, Sotiropoulou G. (2017) Elimination of *Klk6* inhibits the development and progression of non-melanoma skin cancer *in vivo* by suppression of skin inflammation. *The 7th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2017)*, Université F. Rabelais, Tours, France, 26-29 September 2017
10. Kiritsi D, Pampalakis G, Zingkou E, Franzke C-W, Valari M, **Sotiropoulou G.** (2017) Enhanced proteolytic activities in Acral Peeling Skin Syndrome: A role of transglutaminase 5 in epidermal homeostasis. *EB2017 - 5th World Conference of EB Research & 4th Conference of EB-CLINET*, 24-27 September 2017, Salzburg, Austria
11. Dimopoulou A, Botsakis K, **Sotiropoulou G**, Vekrellis K, Angelatou F. (2017) Increased phosphorylated (Ser129) alpha-synuclein in substantia nigra and striatum of the dopamine deficient "Weaver" mouse indicates the presence of alpha-synuclein pathology. *"20 years of alpha-synuclein in Parkinson's Disease and related synucleinopathies: from the bedside to the bench and back to the patient",* Athens, Vravrona (Hotel Mare Nostrum), 7-10 September 2017

http://synuclein2017.org

12. **Sotiropoulou G**, Pampalakis G, Charla E, Zingkou E, Jonca N, Schilling O. (2017) Targeting epidermal KLK5 to rescue Peeling Skin Syndrome. *The International Society for Enzymology Annual Conference: Advances in Laboratory Medicine and Pathobiology 2017 (ISE2017),* Santorini Palace, FIra, Thira (Santorini), Greece, June 16-19, 2017
13. Kiritsi D, Pampalakis G, Zingkou E, Franzke C-W, Valari M, **Sotiropoulou G.** (2017) Enhanced proteolytic activities in Acral Peeling Skin Syndrome: A role of transglutaminase 5 in epidermal homeostasis. *The International Society for Enzymology Annual Conference: Advances in Laboratory Medicine and Pathobiology 2017 (ISE2017),* Santorini Palace, FIra, Thira (Santorini), Greece, June 16-19, 2017
14. Pampalakis G, Sykioti V-S, Ximerakis M, Vekrellis K, **Sotiropoulou G.** (2017) KLK6 proteolysis is implicated in the regulation of extracellular alpha-synuclein species and may represent a novel therapeutic approach. *The International Society for Enzymology Annual Conference: Advances in Laboratory Medicine and Pathobiology 2017 (ISE2017),* Santorini Palace, FIra, Thira (Santorini), Greece, June 16-19, 2017
15. Pampalakis G, Zingkou E, Vekrellis K, **Sotiropoulou G.** "Activography": A novel, versatile and easily adaptable diagnostic method for monitoring enzymatic activities in tissues. *The 22nd Congress of the International and European Federations of Clinical Chemistry and Laboratory Medicine of Clinical Chemistry and Laboratory Medicine*, *IFCC-EFLM EuroMedLab2017*; www.athens2017.org), Athens (Greece) June 11-15, 2017
16. Chen H, Sells E, Cui H, Pandey R, Doetschman T, Pampalakis G, **Sotiropoupou G**, Ignatenko NA. "Human tissue Kallikrein 6 enzyme activity regulates epithelial-mesenchymal transition in colon cancer." *The 108th Annual Meeting of the American Association for Cancer Research (AACR)*, Walter E. Washington Convention Center, Washington DC, USA, April 1-5, 2017
17. Pampalakis G, Kiritsi D, Zingkou E, Valari M, Bruckner-Tuderman L, **Sotiropoulou G.** "Elevated epidermal proteolysis and altered KLK5 expression in Acral Peeling Skin Syndrome. "*The 46th Annual Meeting of the European Society for Dermatological Research,* Munich, Germany, September 7-10, 2016

    Abstract published in: Journal of Investigative Dermatology 136 (9): Suppl. 2, S176, 2016
18. Khoury N, Pampalakis G, Zingkou E, Zoumpourlis V, **Sotiropoulou G.*** "KLK6 protease promotes tumor incidence and growth in skin. *The 46th Annual Meeting of the European Society for Dermatological Research,* Munich, Germany, September 7-10, 2016

    Abstract published in: Journal of Investigative Dermatology 136 (9): Suppl. 2, S242, 2016
19. Zingkou E, Pampalakis G, Charla H, **Sotiropoulou G.*** "Combined targeting of skin proteolysis and inflammation as a therapeutic approach for Netherton syndrome." *The 46th Annual Meeting of the European Society for Dermatological Research,* Munich, Germany, September 7-10, 2016

    Abstract published in: Journal of Investigative Dermatology 136 (9): Suppl. 2, S184, 2016
20. **Sotiropoulou G**, Zingkou E, Charla H, Pampalakis G. "Rare skin syndrome provide insights and druggable targets for epidermal overdesquamation and inflammation. **"** "Advances in Laboratory Medicine and Pathobiology 2016". *Under the auspices of the* International Society for Enzymology (ISE), Syros, July 1st to Monday July 4th, 2016
21. Furio L#, Pampalakis G#, Michael IP, Nagy A, **Sotiropoulou G*,** Hovnanian A.* "KLK5 knock-out rescues neonatal lethality and skin defects in a murine model for Netherton syndrome". 1st International Symposium Future in Dermatology: Inflammation. UCD Charles Institute of Dermatology, Dublin, Ireland, 2-3 Oct, 2015

    Abstract published in: Experimental Dermatology 24: 983-986, 2015

22. Furio L, Pampalakis G, Michael I, Nagy A, **Sotiropoulou G**, Hovnanian A. "KLK5 knock-out reverses cutaneous hallmarks of Netherton syndrome". *45th Annual Meeting of the European Society for Dermatological Research*, Rotterdam, The Netherlands. 9-12 September 2015.

    Abstract published in: Journal of Investigative Dermatology 135: S55, 2015

23. **Sotiropoulou G.** "Novel animal models for validation of KLK5 protease as a drug target for overdesquamating/inflammatory skin diseases". *1st International CRS Congress*, Aegli Zappiou, Athens, Greece, May 27-28, 2015

24. Sidiropoulos KG, White NMA, Ding Q, Boulos P, **Sotiropoulou G**, Pampalakis G, Yousef GM. "Kallikrein-related peptidase 6 regulates miR-34a and miRNA-mediated networks to affect oncogenic cell cycle pathways in breast cancer". T*he 104th Annual Meeting of the United States and Canadian Academy of Pathology (USCAP)*, Hynes Convention Center, Boston, MA, USA**,** March 21-27, 2015

    Abstract published in: Laboratory Investigation 95 (S1): 4-573, 2015

25. Sidiropoulos KG, White NM, Bui A, Boulos P, Ding QC, **Sotiropoulou G**, Pampalakis G, Khella H, Yousef GM. "miRNA-mediated anti-metastatic pathway induction by kallikrein 5 over-expression in breast cancer". *The 103rd Annual Meeting* of the *United States and Canadian Academy of Pathology (USCAP),* San Diego, CA, USA, March 1-7, 2014

    Abstract published in: Laboratory Investigation 94 (S1): 34-90, 2014

26. Pampalakis G, Zinghou E, Kalogeropoulou G, Spella M, Stathopoulos G, López-Otín C, **Sotiropoulou G.** "Dual roles of the KLK5 protease in cancer: Insights into the underlying mechanisms". *2nd Advances in Circulating Tumor Cells (ACTC): 2nd International Symposium ACTC-Advances in Circulating Tumor Cells (ACTC): From Basic Research to Clinical Practice* (ACTC2014: www.actc2014.org/), Iberostar Creta Panorama & Mare, Rethymnon, Crete, Greece, 8-11 Oct, 2014

27. Pampalakis G, Zinghou E, Kalogeropoulou G, Spella M, Stathopoulos G, López-Otín C, **Sotiropoulou G.** "Elimination of KLK5 suppresses skin tumor formation by activating epidermal NF-kB"**.** *44th Annual Meeting of the European Society for Dermatological Research* (*ESDR2014*; http://www.esdr2014.org/KPH/), Copenhagen, Denmark, 10-13 Sept 2014

28. Ximerakis M, Pampalakis G, Roumeliotis T, Sykioti V-S, Garbis SD, Stefanis L, **Sotiropoulou G**, Vekrellis K. "Extracellular α-synuclein is resistant to direct KLK6 proteolysis". *The 5th Annual International Symposium on Kallikreins and kallikrein-related peptidases* (*ISK2013*), Li Ka Shing Knowledge Institute at Saint Michael Hospital, Toronto, Ontario, Canada, Sept 28th to Oct 1st, 2013

    Abstract published in: Clinical Chemistry and Laboratory Medicine 52(7): eA21–eA4877, 2014

29. Pampalakis G, Furio L, **Sotiropoulou G**, Hovnanian A. "Generation of the *Klk5-/-* mouse to investigate the roles of KLK5 in skin". *The 5th Annual International Symposium on Kallikreins and kallikrein-related peptidases* (*ISK2013*), Li Ka Shing Knowledge Institute at Saint Michael Hospital, Toronto, Ontario, Canada, Sept 28th to Oct 1st, 2013

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30. **Sotiropoulou G**, Pampalakis G, Smith C, Papadodima O, Chatziioannou A, Zoumpourlis V, Diamandis EP. "Insights into the molecular pathways underlying the dual roles of KLK6 in breast cancer". *The 5th Annual International Symposium on Kallikreins and kallikrein-related peptidases* (*ISK2013*), Li Ka Shing Knowledge Institute at Saint Michael Hospital, Toronto, Ontario, Canada, Sept 28th to Oct 1st, 2013

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31. Zingkou L, Pampalakis G, **Sotiropoulou G.** "Development and characterization of a new polyclonal specific for mouse Klk6". *The 5th Annual International Symposium on Kallikreins and kallikrein-*

related peptidases (*ISK2013*), Li Ka Shing Knowledge Institute at Saint Michael Hospital, Toronto, Ontario, Canada, Sept 28th to Oct 1st, 2013

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33. White NM, Boulos P, Sidiropoulos KG, Pampalakis G, Bui A, Ding Q, Yousef GM, **Sotiropoulou G**. "Kallikrein-related peptidase 6 in breast cancer: effect on miRNA expression and the MAPK pathway". *The 5th Annual International Symposium on Kallikreins and kallikrein-related peptidases* (*ISK2013*), Li Ka Shing Knowledge Institute at Saint Michael Hospital, Toronto, Ontario, Canada, Sept 28th to Oct 1st, 2013

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34. Ximerakis M, Pampalakis G, Roumeliotis T, Sykioti V-S, Garbis SD, Stefanis L, **Sotiropoulou G**, Vekrellis K. "Extracellular α-synuclein is resistant to direct KLK6 proteolysis". *5th Conference on Advances in molecular mechanisms underlying neurological disorders-A Joint Conference of the European Society for Neurochemistry and the Biochemical Society*, Bath, UK, June 23-26, 2013

35. **Sotiropoulou G**, Pampalakis G, Obasuyi O, Papadodima O, Chatziioannou A, Zoumpourlis V. "KLK5 is a putative suppressor of breast cancer and may exert its effects by repressing epithelial-to-mesenchymal transitions and the mevalonate pathway". *Advances in Circulating Tumour Cells (ACTC): From Basic Research to Clinical Practice (ACTC2012)*, Astir Palace Vouliagmeni-Westin Resort, Sept 26-29, 2012

36. **Sotiropoulou G**, Pampalakis G, Smith C, Zoumpourlis V, Diamandis EP. "Molecular basis for the concentration-dependent tumor suppressing effects of KLK6 in breast cancer". *Proceedings of the 103rd Annual Meeting of the American Association for Cancer Research*, Chicago, USA, Mar 31-Apr 4, 2012

37. Pampalakis G, Osahon O, Papadodima O, Chatziioannou A, Zoumpourlis V, **Sotiropoulou G**. "Suppression of the mevalonate pathway and oncogenic signaling may underlie the tumor-suppressing effects of KLK5 in breast cancer". *Proceedings of the 103rd Annual Meeting of the American Association for Cancer Research*, Chicago, USA, Mar 31-Apr 4, 2012

38. Pampalakis G, Osahon O, Papadodima O, Chatziioannou A, Zoumpourlis V, **Sotiropoulou G.** "Biochemical pathways underlying breast cancer suppression by KLK5". *4th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2011): Biochemistry, Molecular Biology and Association to Disease*, Rhodos Palace Hotel, Rhodes Island, Greece, Sept 2-4, 2011

39. Ximerakis M, Karampetsou A, Emmanouilidou E, Pampalakis G, **Sotiropoulou G**, Karalis KP, Stefanis L, Vekrellis K. "Effects of secreted α-synuclein on cellular homeostasis-a focus on glial cells". *The 23rd Biennial Meeting of the International Society of Neurochemistry and the European Society of Neurochemistry (ISN-ESN-2011)*, Athens, Greece, Aug 28-Sept 1, 2011

40. Dimitrakopoulos L, Vorkas PA, **Sotiropoulou G**, Georgoulias V, Lianidou ES. "Development of a methylation-sensitive high resolution melting assay (MS-HRMA) for cystatin C (*CST6*)." *21st International Congress of Clinical Chemistry and Laboratory Medicine, 19th IFCC-EFCC European Congress of Clinical Chemistry and Laboratory Medicine*, Berlin, Germany, May 2011

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44. **Sotiropoulou G,** Pampalakis G, Prosnikli E, Vlahou A, Agalioti T, Zoumpourlis V. "A tumor protective role of kallikrein-related peptidase 6 in breast cancer". *Nature Conferences-The Miami 2010 Winter Symposium: Targeting Cancer Invasion and Metastasis,* Deauville Beach Resort, Miami Beach, FL, USA, Feb 21-24, 2010

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47. Pampalakis G, Prosnikli E, Agalioti T, Vlahou A, Zoumpourlis V, **Sotiropoulou G.** "A tumor protective role for human kallikrein-related peptidase 6 in breast cancer mediated by inhibition of epithelial-to-mesenchymal transition". *7th International Symposium on Minimal Residual Cancer (7th ISMRC),* Astir Palace Vouliagmeni, Athens, Greece, Sept 16-19, 2009

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51. Pampalakis G, Prosnikli E, Agalioti T, Vlahou A, Zoumpourlis V, **Sotiropoulou G.** "Functional roles of human kallikrein-related peptidase 6 in breast cancer". *3rd International Symposium on Kallikreins and Kallikrein-related Peptidases,* TUM, Munich, Germany, Aug 30-Sept 2, 2009

52. Pavlopoulou A, Pampalakis G, **Sotiropoulou G.** "Unraveling the regulatory mechanisms of cystatin M tumor suppressor". *Proceedings of the 100th Annual Meeting of the American Association for Cancer Research*, Denver, Colorado, USA, April 18-22, 2009 [# 09-AB-5187-AACR]

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mesenchymal transition", *EMBO Workshop on "Can epigenetics influence reprogramming and metastatic progression?",* Banz Monastery, Bad Staffelstein, Germany, Oct 6-9, 2008

54. **Sotiropoulou G**, Pampalakis G, Arampatzidou M, Volanis D, Zoumpourlis V. "KLK6 reverses the malignant phenotype of metastatic breast cancer cells", *Proteinases and Their Inhibitors–Recent Developments, 25th Winter School Tiers*, Italy, Feb 27-Mar 2, 2008
55. Kioulafa M, Kaklamanis L, **Sotiropoulou G**, Stathopoulos E, Mavroudis D, Georgoulias V, Lianidou ES. "Prognostic significance of cystatin M (*CST6*) methylation status in early breast cancer". *The XVI meeting of Balcan Clinical Laboratory Federation & Hellenic Congress of Clinical Chemistry*, Athens, Greece,16-18 October, 2008
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