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#### HISTORICAL PERSPECTIVES

# Pioneers in Dermatology and Venereology: an interview with Professor Sarolta Kárpáti

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#### **Conflicts of interest**

None Declared.

#### **Funding source**

None Declared.

#### **Curriculum Vitae**



Sarolta Kárpáti was born in Budapest, Hungary, in 1951.

#### Major studies, titles

 1975 MD at the Semmelweis University, Budapest, Hungary
 1988 PhD: Childhood dermatitis herpetiformis (Heim Pál Hospital for Children)  1995 Habilitation at the Semmelweis University
 1995 DrSc: Autoimmune blistering skin diseases; Hungarian Academy of Sciences

2009 Member of the German Academy of

Sciences Leopoldina

#### Major scholarships

1981 National Scholarship to the Warsaw University,
Department of Dermatology

1988–1991 Humboldt fellowship to the Dermatology
Department of the LMU, Munich

1991–1994 Fogarty fellow later visiting scientist
at the Dermatology Branch, NIH, USA

#### **Working places**

1976–1991 Department of Dermatology,
Heim Pál Hospital for Children, Budapest

1994–now Department of Dermatology, Venereology
and Dermatooncology, Semmelweis University
Senior scientist, Docent, Professor (1994–2004),
Director (2004–2016), Professor (2016–2021),
Professor emerita (2022–)

#### Major academic board positions:

2007–2008 President of the Hungarian
Dermatological Society
2004–2009 Board member of ESDR
2006–2011 Board member of EADV
2006–2008 Executive Committee member of EADV

#### **Major Hungarian Awards**

Széchenyi Professorial Scholarship, Kaposi Mór Award, Semmelweis Ignacz Award.

#### **Major International Awards**

2009 Member of the German Academy of Sciences Leopoldina

2014 EADV: Scientific Achievement Award

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2014 ILDS: Certificate of Appreciation2017 ESDR: Honorary membership

#### Major international editorial memberships:

Current JEADV, JDS, JDDG, EJD, Exp. Dermatol, ADC, Derm.

Review

Earlier JAAD, Hautarzt 2003–2017 Associate Editor: JID

#### What brought you to dermatology?

Originally, I wanted to become an astronomer and later, an internist as my father was. Dermatology seemed to be the visual diagnostic of internal diseases.

#### Who were your most important teachers?

Éva Török: Head of Dermatology Department of the Heim Pal Hospital for Children; my hospital in Budapest. She was an internationally recognized, excellent paediatric dermatologist, a pioneer of the specialty in Hungary. We had a close connection until her rather early death.

Stefania Jablonska: During a scholarship to Warsaw, I learned different laboratory methods for blistering and other autoimmune diseases. She followed my carrier lifelong, and in a few years, I was elected an honorary member of the Warsaw Dermatological Society.

Georg Stingl: The Collegium Hungaricum scholarship at the AKH in Wien was too short for laboratory work, but I learned a lot from his way of scientific thinking and started to reorganize my immune-dermatological knowledge.

Thomas Krieg: With a Humboldt fellowship I moved from my hospital to the LMU Munich to the Clinic of Professor Otto Baun-Falco, who organized, in my view, one of the best dermatology care and education in Europe. Thomas was a silent, demanding scientific dermatologist, who introduced me to the community of international dermatological research. My major task was to identify the ultrastructural binding sites of circulating and tissue-bound autoantibodies in DH, LAD, EBA, gestational and cicatricial pemphigoid. A great win was to learn from Johannes Ring, Michael Landthaler, Wilhelm Stolz, Cornelia Mauch, Michael Meurer and Karin Scharffetter-Kochanek, who all remained very close friends of mine. I left as a corresponding member of the Munich Dermatological Association.

John R. Stanley invited me to the Dermatology Department of the NIH with a Fogarty scholarship, later as a visiting scientist, to work with his team. In his laboratory and at the NIH courses, I was introduced to high level genetic and molecular biological research and performed new laboratory technics. John was an enthusiastic and at the same time sceptical scientist; he could argue passionately but accepted reasoned opinions — also an excellent school. Together with the late Stephen Katz, director of the department, they regularly organized common free-time

programmes including the fellows and their families. In that milieu, we worked in close connection with Masayuki Amagai, Joo Young Roh, Luca Borradori, Kim Yancey, Andrea Cavani, Michael Hertl, Alexander Enk and Mark Udey; all excellent scientists and friends.

#### From whom did you learn most?

Éva Török: Introduction to clinical dermatology.

Stefania Jablonska: Introduction to the scientific laboratory work.

Thomas Krieg: Introduction to the applied science and international research interaction.

John Stanley: Introduction to molecular biology and genetics. Éva Mezey: Introduction to stem cell research (NIH, not dermatologist).

György Marko-Varga: Introduction to the world of proteomics and omics (Lund University, not dermatologist).

#### Please list five of your best publications?

- 1 Kárpáti S, Bürgin-Wolff A, Krieg T, Meurer M, Stolz W, Braun-Falco O. Binding to human jejunum of serum IgA antibody from children with coeliac disease. *Lancet* 1990 Dec 1;336(8727):1335-8. https://doi.org/10.1016/0140-6736(90) 92893-m.
- 2 Sárdy M, Kárpáti S, Merkl B, Paulsson M, Smyth N. Epidermal transglutaminase (TGase 3) is the autoantigen of dermatitis herpetiformis. *J Exp Med.* 2002 Mar 18;195(6):747-57. https://doi.org/10.1084/jem.20011299.
- 3 Bognar P, Nemeth I, Mayer B, Haluszka D, Wikonkal N, Ostorhazi E, John S, Paulsson M, Smyth N, Pasztoi M, Buzas EI, Szipocs R, Kolonics A, Temesvari E, Kárpáti S. Reduced inflammatory threshold indicates skin barrier defect in transglutaminase 3 knockout mice. *J Invest Dermatol.* 2014 Jan;134(1):105-111. https://doi.org/10.1038/jid.2013.307. Epub 2013 Jul 24.
- 4 Mayer B, Silló P, Mazán M, Pintér D, Medvecz M, Has C, Castiglia D, Petit F, Charlesworth A, Hatvani Zs, Pamjav H, Kárpáti S. A unique LAMB3 splice-site mutation with founder effect from the Balkans causes lethal epidermolysis bullosa in several European countries. *Br J Dermatol.* 2016 Oct;175(4):721-7. https:// doi.org/10.1111/bjd.14646. Epub 2016 Aug 8.
- 5 Betancourt LH, Gil J, Kim Y, et al. The human melanoma proteome atlas defining the molecular pathology. *Clin Transl Med.* 2021; 11(7): e473.. https://doi.org/10.1002/ctm2. 473.PMID: 34323403

## Have you ever been president or in the leadership of an academic society?

ESDR: board member (2004-2009).

EADV: board member (2006–2011) and executive committee member (2006–2008).

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Hungarian Dermatological Society; president (2007–2008).

## What was your greatest achievement in your professional life?

The dermatitis herpetiformis (DH) - transglutaminase (TG) story (selection). With the IF technique in my hand, I wanted to explore why only DH patients have no circulating autoantibodies binding to the site of skin pathology, while most of the DH kids had serum IgA against the smooth muscle layer of monkey oesophagus substrate, which is an entrance to the gut (identified soon as endomysium antibody by Beutner and Chorzelski). So, I started to study IgA also in the underlying coeliac disease on the jejunum of DH patients. My first observation was description of the circulating and identically tissue-bound anti-jejunal IgA autoantibodies in DH (IID, 1986,1988) - later also in coeliac disease (Lancet, 1990), and I analysed these findings also by immune ultrastructural (IEM) studies (IID 1991, Gut 1992). After the identification of TG2 as autoantigen of coeliac disease by Schuppan in 1998, it seemed to be reasonable to look (similarly to pemphigus forms) to search for other TG-s in DH skin pathology. Thomas Krieg connected me with the TG research group of Mats Paulsson in Cologne. With his group and my PhD student, Miklós Sárdy, we identified the TG3 as autoantigen of DH (JExpMed, 2002). The presence of TG3 in DH-associated cutaneous vasculitis (JEADV, 2005) and earlier IEM data (Arch Dermatol, 1990) on IgA positive 'DH bodies' with immune complex structures in the skin, confirmed the further search for circulating TG3-IgA immune complexes (JID, 2016) in DH. The description of the cryofibrinogenaemia (JEADV 2016) and the fibrinolytic pathology (JDS 2016) in the patients brought further new information about the disease. Currently, I am working on the background of the multiplex transglutaminase pathology in DH and also in other diseases.

## What was your greatest disappointment in your professional life?

Just when I began my 12-year chairmanship at the Semmelweis University, the Ministry of Health closed the state authority-funded National Dermato-Venereology Center (OBNI), which was operated for more than 50 years in a personal union with the clinic, contributing to the common education, clinical care and research tasks. With that, the pay of 51 staff members was ceased, while the majority of their tasks remained in the clinic. That was the hardest time in my professional life.

# Can you tell us any funny episodes from your professional life?

During my scholarship in Warsaw, I was honoured by a solo ticket from my colleagues to the theatre performance by the young Karol Wojtyla (Johannes Paulus II, the idol of the nation, played with the music of Krzysztof Penderecki) in Krakow. So, I flew there but fell when I arrived in the theatre, and although I sat down through the play, I could not even stand up by the end. The kind aid arrived in the morning from Krakow Dermatology Clinic, who took me to first aid, then with a non-moving plaster also to the airport. After a friendly farewell, I left, however, my plane could not land in Warsaw, and after long-lasting hours I was again in Krakow. I will never forget the kind hospitality of Docent Starzycki's family — my plane could depart only the next day.

#### Who is your favourite composer, writer or painter?

Writer: Sándor Márai, also, Péter Esterházy or Thomas Mann, sometimes Franz Kafka and many others, like in honour of Johannes Ring, Platon speaking as Socrates (*Phaidon*, Socrates' defence).

Composer: Franz Liszt, Ludwig van Beethoven, Richard Wagner, Béla Bartók, on other days Frédéric Chopin, Wolfgang Amadeus Mozart, Johann Sebastian Bach . . .

Painter: Monika Hajósy (HU) – but I enjoy and learn from works of Italian, French, German, Dutch, Austrian, Spanish painters from very different epochs of human history.

### Apart from dermatology, what is your major interest?

My family – and that includes various interests and activities. Recently, also cloud observation; I am a proud member of the British Cloud Appreciation Society (interestingly, the cloud nomenclature is very similar to the dermatological one).

# Who would you list as the most influential dermatologists in history?

Moritz Kaposi: Significant contribution to the early clinical dermatology in Europe.

David Gruby: Founder of cutaneous mycology, and a very colourful personality.

Albert L.S. Neisser not only discovered the causative microbe of gonorrhoea, but founded the first society to treat STIs.

Stephen Rothman considered as the founder of investigative dermatology in the USA.

Rudi Harold Cormane introduced immunofluorescence through the verification of autoimmune blistering diseases into dermatological diagnostics.

Stefania Jablonska: I admire her broad lifelong pioneering and international leading activities, and remember the described novel autoimmune blistering diseases, scleroderma forms, the role of HPV in cancers and in EDV.

Otto Braun-Falco: It was probably his personality, knowledge and education that made him raise most department heads in his country, and also some in Europe.

Bernard Ackerman established a comprehensive histological differential diagnosis of inflammatory skin diseases.

Stephen I. Katz: In addition to his scientific activities in skin immunology, we have to remember his significant personal

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contribution in his leading positions and his friendly, international collaboration with the dermatological communities worldwide.

Nancy Burton Esterly: Excellent paediatric dermatologist, founder of the specialty in the USA, also the founder of the Society for Pediatric Dermatology.

# Whom would you list among the top 10 of living dermatologists?

This is again a very personal selection, I have too many candidates, but I will mention just 10 of them as requested:

Rudolf Happle: By his exact clinical observations on the cutaneous mosaicism, he could interpret the pathology of several unusual skin diseases, opening novel ways of science to explain inherited, congenital and acquired diseases.

Jouni Uitto established an outstanding dermato-genetic school in the USA by introducing the diagnostic and prenatal diagnostic mutation analysis in inherited skin diseases.

Louis Dubertret: Besides his excellent scientific and clinical activities in Paris, he created the René Touraine Foundation, an international non-profit, non-governmental organization that aims to develop partnerships between stakeholders in therapeutic progress to improve the quality of care in dermatology in Europe and around the world, already before the establishment of ESDR and EADV.

Masayuki Amagai: Together with Takashi Hashimoto and Hiroshi Shimizu, he is one of the three scientifically and clinically outstanding fellows of Takeji Nishikawa from the Keio University. Dr. Amagai cloned the pemphigus vulgaris autoantigen, unravelled the immunological background of the disease, and by developing different autoimmune and other mouse model systems he significantly contributed to understanding the pathology of skin barrier and immunological diseases generally.

Wilhelm Stolz: This very knowledgeable and humble colleague majorly contributed to the development of the very first, every day used hand instrument, the dermatoscope, the favourite equipment of dermatologists, and proved its usefulness by mathematical algorithms, elaborating also the first scoring system, and with that, I consider him as the founder of a new subspecialty within the dermatology.

Georg Stingl: An outstanding immunodermatologist- while considered as pioneer in cutaneous antigen presenting, his activities include the latest immunology related to skin, cutaneous infections and cancers. He has been serving at highest positions of European, American and international academic and scientific societies and committees. Beside his professional career he is a devoted teacher.

Leena Bruckner-Tuderman: Besides outstanding clinical and academic activities, her science includes the deep biology of

basement membrane and extracellular matrix, the epithelial-mesenchymal communication and cell-matrix interactions. Her research on molecular genetics and disease mechanisms of skin disorders has determined also her clinical science in the development of cell, gene and protein-based therapies also in international collaborations.

Johannes Ring: Not only an internationally highly recognized allergo-immunologist and dermatologist but also a philosopher. Clinical dermatologist or director, congress president or president with ongoing activities in leading dermatological, clinical, scientific and allergological societies, successful editor he always tried to present us, dermatologists, including the youngest generation, the supportive power of philosophy, history, art and music in our work .

Barbara A. Gilchrest: The dermatological scientist from the Harvard and BMU worked on cellular responses to UV irradiation in melanogenesis and DNA damage responses, served in leadership positions for the major dermatological organizations and on the Board of Scientific Counsellors of the NCI. To train and motivate young researchers, as editor-in-chief she involved the residents in the editorial work and in the regular educational publication programme of the JID.

John McGrath: A very dynamic, internationally active dermatologist and geneticist, who has not only unravelled the background of known and novel inherited skin diseases, but analysed the complexity of associated inflammatory and immunological events. He is also working on novel non-cell-non-gene therapies. Working together with specialists from less developed areas of dermatology, he is also supporting the quality care and skin science development in that part of the world.

# What will be the greatest problem for dermatology in the next 10 years?

Pandemics and infectious diseases in general, also in our specialty.

### What will be the next breakthrough in the coming 10 years in dermatology?

Some or all of the following three challenges:

Controlling and restoring the skin microbiome and the skin barrier

Understanding and blocking skin cancer development and progression.

Getting closer to compensate or prevent the burden of inherited skin diseases.

\*Note: The *Pioneers in Dermatology and Venereology* interview was conceived and conducted by Johannes Ring.