BIOGRAPHICAL SKETCH			
NAME Holländer, Georg Andreas Peter	POSITION TITLE Full Professor of Paediatric Immunology, University of Basel, Switzerland; Head of Department and Action Research Professor of Paediatrics, University of Oxford, UK;		
ORCID ID	0000-0002-8790-0874		
EDUCATION/TRAINING/INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Basel University Medical School	M.D.	1977-1983	Medicine
Fellowship in Pulmonary Medicine, The Children's Hospital, Harvard University, Boston, USA		1985-1986	Pediatric Pulmonology
Specialty training in Paediatrics, Basel Children's Hospital, Switzerland		1986-1989	Pediatrics

Positions

1983	Student training, Basel Institute for Immunology, Basel, Switzerland
1985	Postdoctoral Fellowship, Basel Institute for Immunology, Basel, Switzerland
1987	Visiting Scientist, Basel Institute for Immunology, Basel, Switzerland
1989 - 1994	Postdoctoral Fellowship, Division of Pediatric Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA
1994 - 1995	Instructor, Harvard Medical School, Boston, USA
1995 - 2000	Assistant Professor, Harvard Medical School, Boston, USA
1995 - 1999	Consultant, Basel Children's Hospital, University Clinics, and Research Group Leader, Department of Research, University Clinics, Basel
1996 - 2004	Scientific Head of the Animal Facility, Department of Research, University Clinics, Basel
1999 - 2010	Head of Research, Basel University Children's Hospital.
1999 - 2003	Tenured Professor (*strukturelles Extraordinariat*), Basel University
2000 - 2007	Member of the Board of the Department of Clinical-biological Sciences
Since 2003	Full Professor Molecular Medicine in Pediatrics (*Ordinariat*), Basel University
Since 2003	Founding Member, Institute for Research in Immunology and Cancer, University of Montreal, Canada
Since 2007	Visiting Professor, Institute for Genome Research, University of Tokushima, Japan
Since 2010	Full Professor Paediatric Immunology (*Ordinariat*), Basel University, and Hoffmann and Action Medical Research Professor of Developmental Medicine, University of Oxford, United Kingdom
Since 2014	Head of the Department of Paediatrics, University of Oxford, United Kingdom
Since 2019	Director of the Botnar Research Centre for Child Health, ETH Zurich & University of Basel, and Hoffmann and Action Medical Research Professor of Developmental Medicine, University of Oxford, United Kingdom

Major scientific achievements

Georg Holländer's research focuses on the development and function of thymic epithelial cells (TE) and has contributed to a detailed immunological understanding of these cells in both health and disease. He demonstrated for the first time that the correct differentiation and growth of TE requires inductive signals from early maturing thymocytes and that these are necessary for the sustained ontogeny of self-tolerant T cells (Nature, 1995; Immunity, 1995; Nature Immunology 2014). This work together with organ developmental studies provided explicit cellular and functional evidence of the lympho-stromal crosstalk essential for establishing a regular composition and architecture of the thymic microenvironment (Development 2000).

Follow-up studies identified Wnt glycoproteins secreted by thymic epithelial cells and thymocytes to regulate in an autocrine and paracrine fashion the expression of Foxn1, a master regulator of TE differentiation and function (Nature Immunology, 2002). Novel transgenic animal models, single cell sequencing and mapping of chromatin accessibility have now identified genome-wide the direct gene targets of Foxn1 and demonstrated that this transcription factor directly choreographs essential aspects of lymphocyte-stromal cross-talk during early and late stages of intra-thymic T lymphoid development, including lineage commitment and antigen-receptor selection (Nature Immunology, 2016). These findings complement earlier work by Holländer linking the Autoimmune Regulator (Aire) to thymocyte selection (JI, 2000) and demonstrating the signals that control the presence of Aire positivity in epithelia of the thymic medulla (Immunity, 2008). Pioneering work has now precisely quantified in Aire-positive TE at population and single cell level the number of promiscuously expressed tissue-restricted antigens and relates this phenomenon to specific epigenetic mechanisms such as histone modifications and micro-RNA expression (Genome Research,2014). These studies have directed a new series of genomic, proteomic and epigenetic studies that interrogated the different influences controlling promiscuous gene expression. For this, several newly developed models with loss and gain of gene function have been created and analysed. One of these mice established the role of microRNA in the maintenance of TE and their capacity to effect promiscuous gene expression (Nature Immunology, 2011; JI, 2012).

Work in parallel characterised the mouse TE progenitor that, upon transfer, fully reconstitutes the thymic epithelial microenvironment (Nature Immunology, 2002), established a novel lineage map (PNAS, 2014, European Journal of Immunology 2016), and identified tumor necrosis factor (TNF)-β to physiologically limit TE growth and function established that the physiological size of the medullary TE compartment is suboptimal to effect negative selection and thus depends on the production of regulatory T cells to reduce the autoreactive potential of regularly selected T cells in the periphery (Nature Immunology, 2014).

Using experimental bone marrow transplantation models, the work of Hollander demonstrated that TE serve as principle targets of Graft-versus-host-disease (GVHD) and, consequently, diminish their Aire expression. This results in a restricted representation of tissue-specific antigens, a lack in appropriate T cell selection, and, ultimately, in rededuc survival and the persistence of self-reactive T cells responsible for the autoimmune manifestations of chronic GVHD (Blood, 2015).

Work by Holländer identified interleukin-2 to be monoallecically expressed in a non-imprinted regulatory mode to achieve precise expression upon T cell activation, thus preventing anergy, aberrant T cell activation and autoimmunity (Science 1998).

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/54940244/?sort=date&direction=ascending

Research output last 5 years

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2. Shitara S, Hara T, Liang B, Wagatsuma K, Zuklys S, Holländer GA, Nakase H, Chiba T, Tani-Ichi S, Ikuta K. IL-7 Produced by Thymic Epithelial Cells Plays a Major Role in the Development of Thymocytes and TCRγδ+ Intraepithelial Lymphocytes. J Immunol. 2013 May 17. J Immunol. 2013; 190: 6173-9.
3. Dertschnig S, Nusspaumer G, Ivanek R, Hauri-Hohl MM, Holländer GA*, Krenger W*. Epithelial cytoprotection sustains ectopic expression of tissue-restricted antigens in the thymus during murine acute GVHD. Blood. 2013, 122: 837-41. *=shared senior authorship.
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5. Jenkinson et al. TRAF3 enforces the requirement for T cell crossstalk in thymic medullary epithelial development. Proc Natl Acad Sci U S A. 2013, 110: 21107-12
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29. Handel AE, Irani SR, Holländer GA. Grand Central: The role of central tolerance for induction of central nervous system autoimmunity. Nat Rev Neuro. *In press*

Major scientific achievements

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