BIOGRAPHICAL SKETCH

NAME: Janovjak, Harald

POSITION TITLE: EMBL Australia Group Leader

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Biozentrum, University of Basel, Switzerland	Dipl./M.S.	11/2002	Molecular Biology
University of Technology Dresden, Germany	Dr.	12/2005	Biophysics, Biology
University of California Berkeley, USA	Post-doctoral	06/2010	Optogenetics, Neuroscience
Ludwig Maximilian University, Munich, Germany	Post-doctoral	02/2011	Optogenetics, Neuroscience

A. Personal Statement

My research has always revolved around understanding cell signaling and animal physiology with new and innovative approaches. I followed this common thread throughout my career that brought me to the fields of protein folding/instrumentation development, optogenetics/neuroscience and synthetic biology/regenerative medicine. My work resulted in well-cited publications at all stages of my career (February 1, 2020: 54 total publications, 38 peer-reviewed research articles, 10 review articles/perspectives and 7 book chapters/protocol articles/books; H-index 22 (WebOfScience); >3500 citations (GoogleScholar)). For more information, also see: http://www.janovjak-lab.com.

B. Positions and Honors

Academic positions:

2011 - 2017 Assistant Professor in Synthetic Physiology
Institute of Science and Technology Austria (IST Austria)

2018 - Group Leader, EMBL Australia Partnership Laboratory (EMBL Australia)
Monash University, Faculty of Medicine, Nursing and Health Sciences

2018 - Group Leader, Australian Regenerative Medicine Institute (ARMI)
Monash University, Faculty of Medicine, Nursing and Health Sciences

Other positions:

2005 - 2006 Principle Scientist *ad interim*, nAmbition GmbH, Dresden, Germany
(now part of JPK Instruments GmbH and Bruker Corp).

Honors:

2002 Graduate research with highest honors
2005 Doctorate with highest honors (*summa cum laude*)
2007 - 2009 Long-term Fellow of the European Molecular Biology Organization
2010 Returning Fellows Grant, Ministry of Science and Education, Düsseldorf
2011 Human Frontier Science Program Young Investigators Grant
2011 European Union Seventh Framework Programme Career Integration Grant
2018 JDRF/Macquarie Group Foundation Future Research Leader
2020 Dean's Senior Leadership Course Award

Fellowships:

2007 Post-doctoral Fellowship, German Research Foundation
2007 Young Investigator Fellowship, Swiss National Science Foundation
2007 - 2009 Long-term Fellowship, European Molecular Biology Organization

Memberships:

2005 Biophysical Society (Germany)
2007 Biophysical Society (US)

2011 Competence Center Cancer Research (CCC, Austria)
2011 Biophysical Society (Austria)
2012 Austrian Association of Molecular Life Sciences and Biotechnology (OEGMBT)
2012 Society for Neuroscience (SFN, US)
2013 American Society for Cell Biology (ASCB)
2014 European Association for the Study of Diabetes (EASD)

Service at Monash University:
2020 Member, Organizing Committee, EMBL Australia PhD course
2019 - 2020 Chair, Monash Histology Platform User Group
2019 - 2020 Member, Monash Histology Platform Steering Group
2018 - 2020 Member, EMBL Australia Travel Grant Selection Committee
2018 - 2020 Chair, ARMI External Speaker Series Committee
2018 External assessor, ARMI Honours Thesis Projects

Reviewer for funding agencies:
Agency for Science, Technology and Research Singapore (A*STAR), Alexander von Humboldt-Foundation (AvH), Australian Research Council (ARC), Boehringer Ingelheim Foundation (BIF), Diabetes Australia, European Research Council (ERC), French National Alliance for Life and Health Sciences, French National Cancer Institute, German-Israeli Foundation for Scientific Research and Development, German Research Foundation (DFG), Israel Science Foundation (ISF), L'Agence nationale de la recherché (ANR), Ministry of Education and Science of the Russian Federation, National Health and Medical Research Council (NHMRC), Netherlands Organisation for Scientific Research (NWO), Research Foundation Flanders (FWO).

Selected keynote or invited talks (from 49 invited talks in the years 2014-2019):
2019 Neuroplasticity - Systems, Synapses and Tools Symposium, Hobart, TAS
2019 13th Australian Peptide Conference, Port Douglas, QLD
2019 Charles Perkins Centre, University of Sydney, NSW
2019 University of New South Wales, Sydney, NSW
2019 Baker Heart and Diabetes Institute, Melbourne, VIC
2018 International Symposium on Growth Factors in Disease and Therapy, Wenzhou, China
2018 Genetic Manipulation of Neuronal Activity V, Janelia Research Campus, USA
2018 Keynote @ Gordon Research Conference FGFs in Development & Disease, Ventura, USA
2018 Gordon Research Conference Photosensory Receptors and Signal Transduction, Il Ciocco, Italy
2018 Department of Chemistry, Stanford University, USA
2017 Keynote @ The VIP-PACAP Congress 2017, Hong Kong SAR, China
2017 Keynote @ Paul Ehrlich Symposium in Medicinal Chemistry, Vienna, Austria
2016 26th ISN-ESN Biennial Meeting, International Society for Neurochemistry, Paris, France
2016 Genetic Manipulation of Neuronal Activity IV, Janelia Research Campus, USA
2016 17th International Conference on Retinal Proteins, Potsdam, Germany
2015 BIOSS Centre for Biological Signalling Studies, Freiburg, Germany
2015 Ludwig Institute for Cancer Research, Oxford, UK
2014 16th International Congress on Photobiology, Cordoba, Argentina
2014 Salk Institute for Biological Studies, San Diego, USA

C. Contributions to Science

1. How do membrane proteins fold and unfold?
Protein folding is not yet understood. The discovery of parallel folding and unfolding pathways highlights that single-molecule techniques are required to address the folding problem. As a graduate student at TU Dresden, I applied forces generated by atomic force microscopy (AFM) to denature single membrane proteins. I was able to measure the energy stabilizing α-helices in the light-driven proton pump bacteriorhodopsin and provided the first experimental measure of roughness in a membrane protein's energy landscape. I also conducted the first combined thermal and mechanical unfolding experiment and, through instrumentation development, probed protein visco-elastics and extended the dynamic range of the technique. We also followed single proteins as they proceeded through the folding process revealing detailed insights into otherwise inaccessible kinetics and pathways. To complement the experiments, I started a collaboration with Marek Cieplak that yielded the first theoretical study of mechanical membrane protein unfolding.

Key references:

"Transmembrane helices have rough energy surfaces"
H. Janovjak, H. Knaus & D.J. Müller
Journal of the American Chemical Society (2007) 129: 246-247.

"Observing folding pathways and kinetics of a single sodium-proton antiporter from *E. coli*"
A. Kedrov, **H. Janovjak**, C. Ziegler, W. Kühlbrandt & D.J. Müller
Journal of Molecular Biology (2006) 355: 2-8.

"Hydrodynamic effects in fast AFM single molecule force measurements"
H. Janovjak, J. Struckmeier & D.J. Müller
European Biophysics Journal (2005) 34: 91-96.

"Probing the energy landscape of the membrane protein bacteriorhodopsin"
H. Janovjak, J. Struckmeier, M. Hubain, M. Kessler, A. Kedrov & D.J. Müller
Structure (2004) 12: 871-879 (with front cover).

"Unfolding pathways of native bacteriorhodopsin depend on temperature"
H. Janovjak, M. Kessler, D. Oesterhelt, H.E. Gaub & D.J. Müller
EMBO Journal (2003) 22: 5220-5229.

2. Can we control nerve cell activity using light?

Genetically-targeted, light-gated ion channels can drive activity in selected nerve cells and thereby probe neural circuits. As a post-doctoral fellow at UC Berkeley, I created novel ion channels that are controlled by photochromic tethered ligands. I used protein engineering to redesign a glutamate receptor into a light-activated, K^+-selective ion channel called HyLighter. This novel functionality was achieved by inserting a functional domain of a bacterial protein into its mammalian homologue. When expressed in neuronal cultures, brain slices and zebrafish and activated by a brief light pulse, HyLighter stably but reversibly inhibits action potential firing and behavior. The low light intensity required for HyLighter activation and its bi-stability proves advantageous for the dissection of neural circuitry *in vivo* where activity is first silenced and behavior is then analyzed in free animals. Motivated by the functional compatibility of a K^+ channel pore with a glutamate receptor demonstrated in HyLighter, I discovered a new family of glutamate receptors in lower invertebrates that carry a K^+ selectivity filter in their pore domains.

Key references:

"A modern ionotropic glutamate receptor with a potassium-selectivity signature sequence"
H. Janovjak, G. Sandoz & E.Y. Isacoff
Nature Communications (2011) 2: 232.

"A light-gated, potassium-selective glutamate receptor for the optical inhibition of neuronal firing"
H. Janovjak, S. Szobota, C. Wyart, D. Trauner & E.Y. Isacoff
Nature Neuroscience (2010) 13: 1027-1032.

3. Optical control of cellular signals and cell behavior

The impact of light control on cell and developmental biology has been limited. In my independent laboratory, we established optogenetic tools that control cell signaling pathways with spatial and temporal precision. We pioneered light-activated receptor tyrosine kinases and light-activated serine/threonine kinases (called 'Opto-RTKs' and 'Opto-RSTKs', e.g. 'Opto-EGFR', our light-activated EGF receptor). We and others utilize these receptors to non-invasively control key signaling cascades (e.g. MAPK or PI3K) and cell behaviors (e.g. cell proliferation and differentiation) with unprecedented precision in different areas of cell and developmental biology. To advance the field as a whole, we share published (and often also unpublished) materials 'with-no-strings-attached', and groups at ETH, CNRS, Yale, CalTech, UCSF, Columbia, McGill, Princeton, UCL, to just name a few institutions, requested our constructs. We further pioneered the application of optogenetics to proteins whose function is currently not known. A large number human G-protein coupled receptors (GPCRs) are classified as 'orphans' as their ligands, downstream pathways and physiological roles remain elusive. To identify downstream signals of these proteins and to establish tools with which they can be studied in the relevant cellular context, we reengineered almost all human orphan GPCRs to be activated by light. Our results show that, in contrast to recent models, many orphan GPCRs are signaling-competent proteins that activate distinct signaling pathways.

Key references:

"Light-activated chimeric GPCRs: Limitations and opportunities"
A.M. Tichy, E.J. Gerrard, P.M. Sexton & **H. Janovjak**
Current Opinion in Structural Biology (2019) 57: 196-203.

"Engineering strategy and vector library for the rapid generation of modular light-controlled protein-protein interactions"
A.M. Tichy, E.J. Gerrard, J.M.D. Legrand, R.M. Hobbs & **H. Janovjak**
Journal of Molecular Biology (2019) 431: 3046-3055.

"Optical functionalization of human Class A orphan G-protein coupled receptors"
M. Morri, I. Sanchez-Romero, A.M. Tichy, S. Kainrath, E.J. Gerrard, P. Hirschfeld, J. Schwarz & **H. Janovjak**
Nature Communications (2018) 9: 1950.

"Green light-induced inactivation of receptor signaling using cobalamin-binding domains"
S. Kainrath, M. Stadler, E. Reichhart, M. Distel & **H. Janovjak**
Angewandte Chemie Int. Ed. (2017) 56: 4608-4611.

"A phytochrome sensory domain permits receptor activation by red light"
E. Reichhart, A. Ingles-Prieto, A.M. Tichy, C. McKenzie & **H. Janovjak**
Angewandte Chemie Int. Ed. (2016) 55: 6339-6342.

"Spatio-temporally precise activation of engineered receptor tyrosine kinases by light"
M. Grusch, K. Schelch, R. Riedler, E. Reichhart, C. Differ, W. Berger, A. Ingles-Prieto & **H. Janovjak**
EMBO Journal (2014) 33: 1713-1726.

We filed three patent applications connected to this work.

4. Light permits a new paradigm in drug screening

We and others proposed that the non-invasive nature of optogenetics may be exploited to create new experimental paradigms in small molecule screening. In my independent laboratory, we recently demonstrated the first optogenetics-assisted small molecule screen. In our 'all-optical' system, light acted both as activator and read-out to obviate the use of assay chemicals (e.g. peptide ligands or reagents for read-out), to limit the number of required operational steps (e.g. solution exchange or other invasive actions) and to improve specificity. Using the all-optical platform, we identified AV-951 (Tivozanib) as a potent and selective inhibitor of ROS1, an orphan kinase that we for the first time activated with light in the absence of the unknown ligand. Optogenetics-assisted screening is transferable to many other classes of drug targets, including voltage-gated ion channels.

Key references:

"All-optical miniaturized co-culture assay of voltage-gated Ca^{2+} channels"
V. Agus & **H. Janovjak**
Methods in Molecular Biology (2019) in press.

"Optogenetic methods in drug screening: Technologies and applications"
V. Agus & **H. Janovjak**
Current Opinion in Biotechnology (2017) 5: 8-14.

"Light-assisted small molecule screening against protein kinases"
A. Ingles-Prieto, E. Reichhart, M.K. Muellner, M. Nowak, S.M. Nijman, M. Grusch & **H. Janovjak**
Nature Chemical Biology (2015) 11: 952-954.

We filed one patent application connected to this work.

A complete list of published work can be found at: http://www.ncbi.nlm.nih.gov/pubmed?term=Janovjak[Author]

D. Research Support

In my role as an independent group leader I have acquired a total of ~$6,310,000 competitive grant funding (2010-2019; excluding scholarships and fellowships awarded to my group members). I was the lead investigator on ~$5,210,000 of this funding. Major research grants included an NHMRC 2019 Ideas Grant ($460,000, CI-A), an ARC 2020 DP grant ($598,000, CI-A), the Returning Fellows Award Germany ($1,975,000, CI-A), HFSP Young Investigator Grant ($1,400,000, lead CI) and Austrian Science Fund project grants ($233,000, $292,000 and $1,027,000 as CI-A or node head). In addition, the Commonwealth Scientific and Industrial Research Organisation (CSIRO) recently funded a collaborative project with $887,000.