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## Hendrik Poeck, MD

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### Start Year

2013

### Education

Ludwigs-Maximilians-University, Munich, Germany; Harvard Medical School, Boston, MA; University of Cape Town, Capetown, SA.

Pattern-recognition receptors (PRRs), including Toll-like receptors (TLRs), NOD-like receptors (NLRs), RIG-I like receptors (RLRs) and cytosolic DNA sensors (cyclic GMP-AMP (cGAMP) synthetase (cGAS), stimulator of interferon genes (STING), absent in melanoma 2 (AIM2)) and others involved in pathogen recognition are critical for host defense. Furthermore, there is emerging evidence that PRRs including TLRs and NLRs can influence the development of acute graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT), although the mechanisms governing this response remain poorly understood. Understanding the processes that help prevent GVHD while preserving graft-versus-tumor activity (GVT) against hematopoietic malignancies will allow for the clinical exploitation of strategies for improving allo-HSCT outcome.

We have provided recent evidence that activation of the NLRP3 inflammasome — a multiprotein complex that regulates the production of bioactive Interleukin-1 $\beta$  and IL-18 — in early conditioning contributes to the development of acute GVHD. Upon irradiation, pathogen-associated molecular patterns (PAMPs) such as enteric bacteria-derived LPS deliver the first signal necessary for pro-IL-1 $\beta$  synthesis. The second signal leading to inflammasome activation and subsequent secretion of bioactive IL-1 $\beta$  is provided by uric acid released from damaged cells. Secreted IL-1 $\beta$  then induces allogeneic Th17 differentiation that contributes to the development of acute GVHD.

Several interesting areas of future study have arisen from this initial discovery, including exploring the role of other innate immune pathways involved in the recognition of commensal microbiota in triggering GVHD, identifying factors that are induced by PRR activation that could selectively reduce GVHD, examining the role of PRRs on GVT activity, and the clinical translation of selective PRR activation as a potential regenerative therapy to boost immune function.

## Awards

Feodor Lynen Scholar for Experienced Researchers (Alexander von Humboldt-Foundation)

## Publications

[Jankovic D, Ganesan J, Bscheider M, Stickel N, Weber FC, Guarda G, Follo M, Pfeifer D, Tardivel A, Ludigs K, Bouazzaoui A, Kerl K, Fischer JC, Haas T, Schmitt-Gräff A, Manoharan A, Müller L, Finke J, Martin SF, Gorka O, Peschel C, Ruland J, Idzko M, Duyster J, Holler E, French LE, Poeck H<sup>\\*#</sup>, Contassot E<sup>\\*#</sup>, Zeiser R<sup>\\*#</sup>. The Nlrp3 inflammasome regulates acute graft-versus-host disease. \*J Exp Med\*. 2013 Sep 23;210\(10\):1899-910. doi: 10.1084/jem.20130084 \\*These authors contributed equally, corresponding authors.](#)

Dann A\*, Poeck H\*, Maihofer C, Endres S, Kalinke U, Knobloch KP, Akira S, Waisman A, Hartmann G and Prinz M. Cytosolic RIG-I-like helicases act as negative regulators of sterile inflammation in the CNS, *Nature Neuroscience* 2011 Dec 4;15(1):98-106. doi: 10.1038/nn.2964 \*These authors contributed equally.

Poeck H\*, Bscheider M\*, Gross O\*, Roth S, Finger K, Hanneschläger N, Schlee M, Rebsamen M, Rothenfusser S, Barchet W, Akira S, Inoue S, Endres S, Peschel C, Hartmann G\*, Hornung V\* and Ruland J\*. Recognition of RNA virus by RIG-I results in activation of CARD9 and inflammasome signaling for interleukin 1beta production. Nature Immunology 2010 Jan;11(1):63-9. *\*These authors contributed equally.*

Besch R\*, Poeck H\* , Hohenauer T, Senft D, Häcker G, Berking C, Hornung V, Endres S, Ruzicka T, Rothenfusser S, Hartmann G. Proapoptotic signalling by RIG-I and MDA-5 results in type I interferon independent apoptosis in melanoma. J Clin Invest. 2009, Aug; 119(8):2399-411 *\*These authors contributed equally.*

Gross O\*, Poeck H\*, Bscheider M, Dostert C, Hanneschläger N, Endres S, Hartmann G, Tardivel A, Schweighoffer E, Tybulewicz V, Mocsai A, Tschopp J, Ruland J. Syk kinase signalling couples to the Nlrp3 inflammasome for anti-fungal host defence. Nature. 2009 May 21;459(7245):433-6. *\*These authors contributed equally.*

Poeck H\*, Besch R\*, Maihoefer C, Renn M, Tormo D, Morskaya S, Kirschnek S, Gaffal E, Landsberg J, Hellmuth J, Schmidt A, Anz D, Bscheider M, Schwerd T, Berking C, Bourquin C, Kalinke U, Kremmer E, Kato H, Akira S, Meyers R, Häcker G, Neuenhahn M, Busch D, Ruland J, Rothenfusser S, Prinz M, Hornung V, Endres S, Tüting T & Hartmann G. 5'-triphosphate siRNA: turning gene-silencing and RIG-I activation against melanoma. Nat Med. 2008 Nov;14 (11):1256-63 *\*These authors contributed equally.*

Poeck H, Wagner M, Battiany J, Rothenfusser S, Wellisch D, Hornung V, Jahrsdorfer B, Giese T, Endres S, Hartmann G. Plasmacytoid dendritic cells, antigen, and CpG-C license human B cells for plasma cell differentiation and immunoglobulin production in the absence of T-cell help. Blood 2004; 103(8):3058-64.

Poeck H, Ruland J. From Virus to Inflammation: Mechanisms of RIG-I-induced IL-1beta production. Eur J Cell Biol. 2012 Jan;91(1):59-64. Epub 2011 Apr 9.

[Poeck H, Ruland J. SYK kinase signaling and the NLRP3 inflammasome in antifungal immunity. J Mol Med \(Berl\). 2010 Aug;88\(8\):745-52. doi: 10.1007/s00109-010-0631-4.](#)

Heidegger S, van den Brink MR, Haas T, Poeck H. The role of pattern-recognition receptors in graft-versus-host disease and graft-versus-leukemia after allogeneic stem cell transplantation. Front Immunol. 2014 Jul 18;5:337. doi: 10.3389/fimmu.2014.00337. eCollection 2014. Review.

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