

Immunität, Immunity

Selbst / Nichtselbst und das Gefahren – Modell der Immunologie Horror autotoxicus and the danger model of immunology

Das Selbst – Nichtselbst Modell (1900), der Begriff Selbsttoleranz (1950) und die Gefahrentheorie (1994)

„Das herkömmliche Verständnis des Immunsystems ist, dass es **Selbst von Nichtselbst** unterscheidet“. Dieses Verständnis wurde 1950 von **Sir Frank Macfarlane Burnet** durch den Begriff **Selbsttoleranz** modifiziert.

Das **Selbst – Nichtselbst Modell** wurde ursprünglich von **Paul Ehrlich** (http://de.wikipedia.org/wiki/Paul_Ehrlich) beschrieben. Er stellte infolge seiner Experimente an Tieren das biologische Prinzip des **Horror autotoxicus** (Furcht vor der Selbsterstörung) auf.

„Im Gegensatz dazu schlägt die **Gefahren Theorie** vor, dass das Immunsystem nicht auf fremde Substanzen reagiert, sondern auf **Situationen, die potentiell schädlich sind**. Das Gefahren Modell wurde ursprünglich von **Polly Matzinger** (1994), beschrieben.“ (Monestier M (2007))

“The conventional understanding of the immune system is that it can differentiate **self from nonself**”. This understanding was modified in 1950 by **Sir Frank Macfarlane Burnet** by the term **self-tolerance**. The **self - non-self model** was originally described by **Paul Ehrlich** (http://en.wikipedia.org/wiki/Paul_Ehrlich). He introduced it as a result of his experiments on animals on the biological principle of **horror autotoxicus** (fear of self-destruction).

“In contrast, the danger theory proposes that the immune system does not react to foreign substances but instead responds to **situations that are potentially harmful**. The danger model was originally proposed by **Polly Matzinger (1994)**, who has described it extensively in several articles”. (Monestier M (2007))
[http://www.ncbi.nlm.nih.gov/pubmed?term=Matzinger%20P\[Author\]&cauthor=true&cauthor_uid=17179963](http://www.ncbi.nlm.nih.gov/pubmed?term=Matzinger%20P[Author]&cauthor=true&cauthor_uid=17179963)

Extrazelluläres Gefährdungspotential, Extracellular danger -> Antibodies, Atikörperbildung

Intrazelluläres Gefährdungspotential, Intracellular danger -> Autoantibodies, Autoantikörper

- ➔ **Borrelien, Immunität** <http://www.erlebnishaft.de/borrelienimmun.pdf>
- ➔ **Complement** <http://www.xerlebnishaft.de/complement.pdf>
- ➔ **Toll like Rezeptoren** http://www.erlebnishaft.de/TLR2_1_3_7_13.pdf
- ➔ **Symbiogenese** <http://www.erlebnishaft.de/symbiogenese.pdf>
- ➔ **Selbstorganisation** http://www.erlebnishaft.de/selbst_muster_nano.pdf

Aber „Beschädigungen sind nicht immer die Ursache einer Immunantwort“. (Pradeu, 2012).
But “damages are not always the cause of an immune response.” (Pradeu, 2012).

Die Nullquantum – Systemtheorie http://www.erlebnishaft.de/selbst_muster_nano.pdf

„Das Ganze ist mehr als die Summe seiner Teile. Aristoteles (384 – 322 v. Chr.)

The whole is more than the sum of its parts.“ Aristoteles (384 – 322 v. Chr.) "Das was aus Bestandteilen so zusammengesetzt ist, dass es ein einheitliches Ganzes bildet, nicht nach Art eines Haufens, sondern wie eine Silbe, das ist offenbar mehr als bloß die Summe seiner Bestandteile." Metaphysik 1041 b 10 (VII. Buch (Z))

„Das Wesen dieser epigenetischen Prozesse besteht folglich darin, dass die Gesamtorganisation eines komplexen multimolekularen Gebildes potentiell in der Struktur seiner Bestandteile enthalten ist, sich aber erst offenbart und damit *wirklich* wird durch ihren Zusammenschluss. ... Der epigenetische Aufbau einer Struktur ist nicht eine *Schöpfung*, er ist eine *Offenbarung*.“

"The nature of these epigenetic processes, therefore, is that the overall organization of a complex multi-molecular structure is potentially contained in the structure of its components, but only *revealed* and thus really will be through their merger. ... The epigenetic construction of a structure is not a *creation*, it is a *revelation*." Quelle, Source: Monod J. (1971) Zufall und Notwendigkeit. Piper. Seite 111

http://www.amazon.de/Zufall-Notwendigkeit-Philosophische-modernen-Biologie/dp/3492019137/ref=sr_1_1/275-0007308-7605448?ie=UTF8&qid=1381403868&sr=8-1&keywords=zufall+und+notwendigkeit

Epigenese, epigenesis: Huismans BD (2007) Das Nullquantum und der 5.Hauptsatz der Thermodynamik. Grin Verlag. <http://www.grin.com/de/e-book/80450/nullquantum-zahlensymbolik-und-struktur>
<http://www.grin.com/de/e-book/71284/lebendigkeit-selbstorganisation-morphogenese-5-hauptsatz-der-thermodynamik>

- ➔ **Standpunkte und Perspektiven** http://www.xerlebnishaft.de/standpunkte_perspektiven.pdf
- ➔ **Mustererkennung, Pattern matching, Selbstorganisation = Beziehungsorganisation**
http://www.erlebnishaft.de/selbst_muster_nano.pdf
- ➔ Spencer HJ (2016) **Quantum Optical Mechanics (QOM)**
www.academia.edu/28244473/Quantum_Optical_Mechanics_QOM_-_JET6 InfinitesimalRev.pdf
106.12 KB [Download](#)
- ➔ **Xenoautophagie** <http://www.xerlebnishaft.de/xenoautophagie.pdf>

[Casadevall A, Pirofski LA](#) (2003) **The damage-response framework of microbial pathogenesis.** *Nat Rev Microbiol.* 1(1), 17-24. <http://www.ncbi.nlm.nih.gov/pubmed/15040176>
«The late twentieth century witnessed the emergence of numerous infectious diseases that are caused by microorganisms that rarely cause disease in normal, healthy immunocompetent hosts. The emergence of these diseases shows that the existing concepts of pathogenicity and virulence do not take into account the fact that both the microorganism and the host contribute to microbial pathogenesis. To address this impediment to studies of host-microorganism interactions, we propose a new theoretical approach to understanding microbial pathogenesis, known as the 'damage-response' framework. «

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[Casadevall A, Pirofski LA](#) (2014) **Ditch the term pathogen.** *Nature* 516, 165
http://www.nature.com/polopoly_fs/1.16502!/menu/main/topColumns/topLeftColumn/pdf/516165a.pdf

[Glisson F](#) (1677) **Tractatus de ventriculo et intestinis. (IRRITABILITY)**
https://play.google.com/store/books/details/Francis_Glisson_Tractatus_de_ventriculo_et_intesti?id=pgY_AAAcAAJ
<https://www.amazon.de/Tractatus-Ventriculo-Intestinis-Praemittitur-Continentibus/dp/1171266596>
<https://catalog.lib.ecu.edu/catalog/2956860>
<http://www.bonhams.com/auctions/22247/lot/105/>

[Brown J](#) (1780) **INCITABILITAS (IRRITABILITAET, Erregungsprinzip) / ERREGBARKEIT (EXCITABILITAS)** [https://de.wikipedia.org/wiki/John_Brown_\(Mediziner\)](https://de.wikipedia.org/wiki/John_Brown_(Mediziner))
„Er teilt die Krankheiten in asthenische Krankheiten und sthenische Krankheiten. Erstere sind die Folge eines zu geringen Reizzustandes und letztere die Folge eines zu starken Erregungszustandes“

[Schedlowski M, Tewes U](#) (1996) **Psychoneuroimmunologie.** Spektrum Akademischer Verlag ISBN-10: 3860252283 ISBN-13:978-3860252284

Louveau A, Smirnov I, Keyes TJ et al. (2015) **Structural and functional features of central nervous system lymphatic vessels.** *Nature*, DOI: [10.1038/nature14432](https://doi.org/10.1038/nature14432)
<http://www.nature.com/nature/journal/vaop/ncurrent/full/nature14432.html>

University of Virginia Health System (2015) **Missing link found between brain, immune system; major disease implications.** *ScienceDaily.* ScienceDaily, 1 June 2015.
<http://www.sciencedaily.com/releases/2015/06/150601122445.htm>

[Mitroulis et al.](#) (2018) Modulation of Myelopoiesis Progenitors Is an Integral Component of Trained Immunity. *Cell*, DOI: [http://dx.doi.org/10.1016/j.cell.2017.11.034](https://doi.org/10.1016/j.cell.2017.11.034)
«Diese Studie hat zum ersten Mal gezeigt, dass eine trainierte angeborene Immunität auf die Vorläufer der zirkulierenden weißen Blutkörperchen im Knochenmark wirkt, die als hämatopoetische Stamm- und Vorläuferzellen (HSVZ) bekannt sind. «

- ➔ **Zytoskelett** <http://www.xerlebnishaft.de/zytoskelett.pdf>
 - ➔ **Das dynamische Genom** http://www.xerlebnishaft.de/dynamic_genome.pdf
 - ➔ **Prione** <http://www.erlebnishaft.de/prione.pdf>
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Extrazelluläres Gefährdungspotential, Extracellular danger

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Cohn, M. 1994. The wisdom of hindsight. Ann. Rev. Immunol. 12, 1-62.

<https://www.ncbi.nlm.nih.gov/pubmed/7516667>

“The take-home lesson is that we need to widen our horizon constantly to make more general concepts that then render the manipulation of the immune system more useful.”

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<https://www.youtube.com/watch?v=RwOZGTFkDtY>

Intrazelluläres Gefährdungspotential, Intracellular danger

..ist ein Sonderfall der Antikörper – Bildung. Dabei werden **Antikörper gegen Bestandteile des Wirtsgewebes nachgewiesen** (Der Wirt ist immer der größere der beteiligten Organisationsformen).
..is a special case of the antibody - formation. Antibodies against components of the host tissue are detected (The host is always the larger of the involved organizational forms).

Beispiele in: <http://de.wikipedia.org/wiki/Autoimmunerkrankung>

Autoimmunerkrankung	Autoantikörper
Rheumatoide Arthritis	Rheumafaktor
Morbus Basedow	Thyreoidea-Rezeptor-Autoantikörper (TRAK)
Systemischer Lupus erythematoses	Anti-Doppelstrang-DNA
Sklerodermie	Anti-Scl-70
Polymyositis / Dermatomyositis	Anti-Jo-1
Sjögren-Syndrom	Anti-SS-A (Ro), Anti-SS-B (=La)
Zöliakie	ARA, EMA, Anti-tTG

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<http://books.google.de/books?hl=de&lr=&id=gqtnHEe3j3C&oi=fnd&pg=PA261&dq=Genetics+and+autoimmunity:+HLA+and+MHC+genes&ots=jeShHwuaja&sig=DdOUTf45x7w-a099ma4fhqNEwc#v=onepage&q=Genetics%20and%20autoimmunity%3A%20HLA%20and%20MHC%20genes&f=false>

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[Shradha Agarwal S](#), [Charlotte Cunningham-Rundles Ch](#) (2009) **Autoimmunity in Common Variable Immunodeficiency**. [Curr Allergy Asthma Rep](#). Author manuscript; available in PMC 2010 Aug 10. Published in final edited form as: [Curr Allergy Asthma Rep](#). 9(5), 347–352. PMID: PMC2919211 NIHMSID: NIHMS224141 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2919211/>

„The most common autoimmune conditions are immune thrombocytopenic purpura and hemolytic anemia, but other autoimmune complications arise, including rheumatoid arthritis, pernicious anemia, primary biliary cirrhosis, thyroiditis, sicca syndrome, systemic lupus, and inflammatory bowel disease. ... The best examples of these include the mutations in CD95 in autoimmune lymphoproliferative disorder, which lead to defective apoptosis and autoimmune cytopenias, and mutations in the IL-2 receptor, signal transducer and activator transcription 5, and forkhead box P3, which lead to loss of functional T-regulatory cells. ... Treatment of autoimmunity includes high-dose immunoglobulins, corticosteroids, selected immunosuppressants, and other immune modulators.“

[Marshall T](#) (2009) Autoimmune Disease explained in 10 minutes
<http://www.youtube.com/watch?v=hcAVeKobsuU>

Conrad K, Schößler W, Hiepe F (2010) Autoantikörper bei organspezifischen Autoimmunerkrankungen. Ein diagnostischer Leitfaden. Pabst Science Publishers, Lengerich, Berlin, Bremen und andere, [ISBN 3-89-967688-2](#)

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“**Rheumatology key messages: Aberrancies of apoptosis can release danger signals, serving as a potential driving force for autoimmunity. Autoimmune diseases may relate to tissue restricted pathology rather than dysfunctions in the immune system itself. The continued presence of danger signals separates autoimmune diseases from ‘physiological’ autoreactivity.**”

Flammer JR, Rogatsky R (2011) Minireview; Glucocorticoids in Autoimmunity: Unexpected Targets and Mechanisms. [Mol. Endocrinol.](#) 25(7) 1075-1086 [Abstract](#) [Full Text \(HTML\)](#) [Full Text \(PDF\)](#)
<http://mend.endojournals.org/content/25/7/1075.full.pdf+html>

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“**The associations have been suspected to be caused by inflammation or brain-reactive antibodies associated with the autoimmune diseases. However, the associations could also be caused by shared genetic factors or common etiologic components such as infections. Infections can induce the development of autoimmune diseases and autoantibodies, possibly affecting the brain. Autoimmune diseases and brain-reactive antibodies should be considered by clinicians in the treatment of individuals with psychotic symptoms, and even if the association is not causal, treatment would probably still improve quality of life and survival.**”

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