



## **Episomal-Persistent DNA in Cancer and Chronic Diseases**

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## **Episomal-Persistent DNA in Cancer- and Chronic Diseases**

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Harald zur Hausen, born 1936, studied Medicine at the Universities of Bonn, Hamburg and Düsseldorf and received his M.D. in 1960. He worked as post-doc at the Institute of Microbiology in Düsseldorf, subsequently in the Virus Laboratories of the Children's Hospital in Philadelphia where he was later appointed as Assistant Professor. After a period of 3 years as a senior scientist at the Institute of Virology of the University of Würzburg, he was appointed in 1972 as Chairman and Professor of Virology at the University of Erlangen-Nürnberg. In 1977 he moved to a similar position to the University of Freiburg. From 1983 until 2003 he was appointed as Scientific Director of the Deutsches Krebsforschungszentrum (German Cancer Research Center) in Heidelberg. He retired from this position in 2003.

He received a number of national and international awards, among them the Robert-Koch-Price, the Charles S. Mott Price of the General Motors Cancer Research Foundation, the Federation of the European Cancer Societies Clinical Research Award, the Paul-Ehrlich-Ludwig Darmstaedter-Price, the Jung-Price, Hamburg, the Charles Rodolphe Brupbacher Price, Zürich, the Prince Mahidol Award, Bangkok, the Raymond Bourguin Award, Paris, the Coley-Award, New York, the Life Science Achievement Award of the American Association for Cancer Research, San Diego, the German Special Order of Merit with Star and the Nobel-Prize for Medicine, 2008. He is elected member of several International Academies, among them the US Academy of Sciences and the Leopoldina in Halle. He received 30 honorary MD and Ph.D. doctorates from the Universities of Chicago, USA, Umeå, Sweden, Prague, Czech Republic, Salford, UK, Helsinki, Finland, Erlangen-Nürnberg and Würzburg, both Germany, Ferrara, Italy, Buenos Aires, Argentine, Madrid, Spain, Melbourne, Australia, Salerno, Italy, Los Angeles, USA, Jerusalem, Israel, Warszawa, Poland, Bucaramanga, Columbia, Besancon, France, Valdivia, Chile, Ljubljana, Slovenia, Antwerp, Belgium, Pisa, Italy, Mount Sinai, New York, USA, Ioannina, Greece, Saigon (Ho Chi-Minh-City), Vietnam, Porto Alegre, Brazil, Athens, Greece, Guadalajara, Mexico, Patras, Greece, Nishny Nowgorod, Russia und Pleven, Bulgaria. In addition, he has been awarded with several international Honorary Professorships.

The division *Episomal-Persistent DNA in Cancer- and Chronic Diseases*, presently headed by Harald zur Hausen, aims at the identification and characterization of disease-associated persistent circular DNA of infectious agents in human materials. Recent studies suggest an involvement of such agents in the development of chronic neurodegenerative diseases (Manuelidis, J. Neurovirol. (2011; 17:131–145). Besides the isolation of such DNAs, central questions are whether and in which way these DNA-sequences and their gene products contribute to the development of certain pathologies. A proof for a direct link between an infection with these agents and a specific disease may open new avenues for intervention (vaccination, identification of patients at risk and targeted therapy).

Numerous novel episomal DNA-sequences related to single-stranded circular DNA viruses have been isolated by this group from milk, bovine sera as well as from different human pathological biopsies (Funk et al., Genome Announc. (2014; 2[4]), Gunst et al., Genome Announc. (2014; 2[4]), Lamberto et al., Genome Announc. (2014; 2[4]), Whitley et al., Genome Announc. (2014; 2[4])). The high degree of homology between isolates from milk, bovine sera and human tissue or serum points at the consumption of bovine meat or dairy products as potential route of transmission. The global epidemiology of some common human cancers (e.g. colon and breast cancer) could suggest a zoonotic origin of these conditions (zur Hausen and de Villiers, 2015).

This division applies molecular biology, cell biology, immunology as well as high throughput methodology (RNA Seq, mass spec, serum scans, protein interaction screening) in order to characterize these novel DNA-sequences and their interactions with the host cell. In addition, seroepidemiological studies are conducted to receive more information on immune interactions between the human host and those agents. The involvement of potentially pathogenic infectious DNA agents in the etiology of malignant and neurological diseases is being studied. This takes into account interactions potentially resulting from the additional exposure to chemical, physical or biological factors. These studies include the level of DNA (genome), RNA (transcriptome) as well as the level of potentially encoded proteins (proteome) and their effects on infected host cells.

Dairy cattle serum and milk factors contributing to the risk of colon and breast cancers.

zur Hausen H, de Villiers EM. *Int J Cancer*. 2015 Feb 3.  
doi: [10.1002/ijc.29466](https://doi.org/10.1002/ijc.29466)

Cancer "causation" by infections--individual contributions and synergistic networks.

zur Hausen H, de Villiers EM. *Semin Oncol*. 2014; 41: 860-75.  
doi: [10.1053/j.seminoncol.2014.10.003](https://doi.org/10.1053/j.seminoncol.2014.10.003)

Novel replication-competent circular DNA molecules from healthy cattle serum and milk and multiple sclerosis-affected human brain tissue.

Whitley C, Gunst K, Müller H, Funk M, zur Hausen H, de Villiers EM. *Genome Announc*. 2014 Aug 28;2(4). pii: e00848-14.  
doi: [10.1128/genomeA.00849-14](https://doi.org/10.1128/genomeA.00849-14)

Mycovirus-like DNA virus sequences from cattle serum and human brain and serum samples from multiple sclerosis patients.

Lamberto I, Gunst K, Müller H, zur Hausen H, de Villiers EM. *Genome Announc*. 2014 Aug 28;2(4). pii: e00848-14.  
doi: [10.1128/genomeA.00848-14](https://doi.org/10.1128/genomeA.00848-14)

Isolation of bacterial plasmid-related replication-associated circular DNA from a serum sample of a multiple sclerosis patient.

Gunst K, zur Hausen H, de Villiers EM. *Genome Announc*. 2014 Aug 28;2(4). pii: e00847-14.  
doi: [10.1128/genomeA.00847-14](https://doi.org/10.1128/genomeA.00847-14)

Isolation of protein-associated circular DNA from healthy cattle serum.

Funk M, Gunst K, Lucansky V, Müller H, zur Hausen H, de Villiers EM. *Genome Announc*. 2014 Aug 28;2(4). pii: e00846-14.  
doi: [10.1128/genomeA.00846-14](https://doi.org/10.1128/genomeA.00846-14)

Epstein-Barr virus stimulates torque teno virus replication: a possible relationship to multiple sclerosis.

Borkosky SS, Whitley C, Kopp-Schneider A, zur Hausen H, de Villiers EM. *PLoS One*. 2012;7(2):e32160.  
doi: [10.1371/journal.pone.0032160](https://doi.org/10.1371/journal.pone.0032160).

Red meat consumption and cancer: reasons to suspect involvement of bovine infectious factors in colorectal cancer.

zur Hausen H. *Int J Cancer*. 2012 Jun 1;130(11):2475-83. Epub 2012 Jan 31.  
doi: [10.1002/ijc.27413](https://doi.org/10.1002/ijc.27413)

The search for infectious causes of human cancers: where and why (Nobel lecture).

zur Hausen H. *Angew Chem Int Ed Engl*. 2009; 48: 5798-808  
doi: [10.1002/anie.200901917](https://doi.org/10.1002/anie.200901917)

HPV vaccine for all.

Michels KB, zur Hausen H. *Lancet*. 2009; Jul 25;374(9686):268-70. Epub 2009 Jul 6.  
doi: [10.1016/S0140-6736\(09\)61247-2](https://doi.org/10.1016/S0140-6736(09)61247-2)

Proliferation-inducing viruses in non-permissive systems as possible causes of human cancers.

zur Hausen H. *Lancet*. 2001; 357(9253):381-4.  
doi: [10.1016/S0140-6736\(00\)03652-7](https://doi.org/10.1016/S0140-6736(00)03652-7)