DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

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Deutsches Krebsforschungszentrum
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Deutsche Krebshilfe

NCT Seminar Series

Speaker	**Matthew Weitzman, PhD** **Associate Director** **Center for Cellular and Molecular Therapeutics** **The Children's Hospital of Philadelphia**
Title	**Genomes in conflict: maintaining genome integrity during virus infection**
Date	**Tuesday, 17th April, 2012**
Time	**10:00 am – 11:00 am**
Location	**NCT – National Center for Tumor Diseases** **Conference Room K2/K3, 2nd floor** **Im Neuenheimer Feld 460, 69120 Heidelberg**
Host	**Prof. Dr. Christof von Kalle**

The cellular surveillance network for sensing and repairing damaged DNA prevents an array of human diseases, and when compromised it can lead to genomic instability and cancer. The carefully maintained cellular response to DNA damage is challenged during viral infection, when foreign DNA is introduced into the cell. Virus replication presents the host cell with large amounts of exogenous genetic material and unusual DNA structures. The battle between virus and host generates a genomic conflict. The host attempts to limit viral infection and protect its genome, while the virus deploys tactics to eliminate, evade or exploit aspects of the cellular defense. Studying this conflict has revealed that the cellular DNA damage response machinery comprises part of

the intrinsic cellular defense against viral infection. I will present recent examples from our lab that demonstrate how viruses manipulate the host cell's DNA repair machinery, and highlight potential outcomes of the conflict for both virus and host. Exploring interactions between viruses and the host DNA repair machinery has revealed novel host responses and insights into cellular pathways of DNA repair.

My lab researches virus-host interactions and uses human DNA viruses as model systems to study fundamental cellular processes. We have shown that viral DNA is recognized and processed by the cellular DNA repair machinery. We have discovered that viruses activate DNA damage pathways and manipulate key cellular regulators of DNA damage recognition and repair. We are interested in how virus interactions with cellular pathways affect genome stability and the implications for gene delivery by viral vectors.

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- Carson, CT, Schwartz, RA, Stracker, TH, Lilley, CE, Lee, DV and Weitzman, MD (2003). The Mre11 complex is required for ATM activation and the G2/M checkpoint. EMBO J, 22,6610-6620.

- Chen, H, Lilley, CE, Yu, Q, Lee, DV, Chou, J, Narvaiza, I, Landau, NR and Weitzman, MD (2006). APOBEC3A is a potent inhibitor of adeno-associated virus and retrotransposons. Curr Bio 16, 480-485.

- Chaurushiya, MS, Lilley, CE, Aslanian, A, Meisenhelder, J, Scott, DC, Landry, S, Ticau, S, Boutell, C, Yates, JR, Schulman, BA, Hunter, T and Weitzman, MD (2012). Viral E3 ubiquitin-mediated degradation of a cellular E3: viral mimicry of a cellular phosphorylation mark targets the RNF8 FHA domain. Mol Cell