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CiViA Center for Immunology of Viral Infections

CiViA lecture

RNA 5' capping with flavin adenine dinucleotide (FAD) protects hepatitis C virus from innate immune responses

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https://isim.ku.dk/research/cohep/?pure=en/persons/221047

Date: Monday 18 September 2023, 11:00 – 12:00

Location: Lakeside auditorium; 1252-204 Eduard Biermann lecture theatre

Abstract:

RNA viruses have evolved elaborate strategies for protection of their genomes, including 5' capping. However, so far no RNA 5' cap was identified for hepatitis C virus (HCV), which causes chronic infection, liver cirrhosis and cancer. Surprisingly, we recently demonstrated that the cellular metabolite flavin adenine dinucleotide (FAD) is used as noncanonical initiating nucleotide by the viral RNA-dependent RNA polymerase resulting in a 5' FAD cap on the HCV RNA. The HCV FAD capping frequency is ~75%, which is the highest observed for any RNA metabolite cap across all kingdoms of life. FAD capping is conserved among HCV isolates for the replication intermediate negative strand and partially for the positive strand. It is also observed *in vivo* on HCV RNA isolated from patient sera and the liver and serum of a human liver chimeric mouse model. Furthermore, we show that 5' FAD capping protects RNA from RIG-I mediated innate immune recognition but does not stabilize the HCV RNA. These results establish capping with cellular metabolites as a novel viral RNA capping strategy, which could be used by other viruses and affect viral treatment outcomes and persistence of infection.