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Cationic lipids efficiently deliver self-amplifying Rep RNA for translation in DC and monocytes

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While host immune defences protect against pathogenic infections, it is critical that host immunity be robust to defend against such infections. Vaccine targeting of dendritic cells (DCs) is an important consideration. Advances in RNA technology have provided high potential in this area, with replicon (Rep RNA) vaccines from either positive or negative RNA strand viruses. Rep RNA will translate self-replicate without producing infectious progeny; this provides high levels of antigen expression of the inserted genes of interest, mimicking viral infections and inducing both humoral and cellular immunity. Synthetic delivery can target dendritic cells (DC), but require replicons from positive strand viruses – negative strand virus replicons require co-delivery of their polymerase. These investigations examined the interaction with Rep RNA from the non-cytopathogenic Classical Swine Fever Virus (CFSV), promoting replication and translation without destroying the targeted DC (a drawback with cytopathogenic replicons). Cationic lipids were assessed for delivery and facilitating Rep RNA translation. Whereas Rep RNA alone interacted inefficiently with DC, the lipids provided a powerful assistance to the DCs for both delivery and translation. It was considered that the cationic nature of the lipids promoted endosomal escape, essential for facilitating Rep RNA translation. However, there was disparity between efficient delivery and translation. Lipids promoting translation were not the most effective for delivery, which relates to observations that Rep RNA delivery requirements are distinct from those for oli RNA. Both *in vitro* and *in vivo* studies have characterized the lipid-mediated binding and delivery of Rep RNA to DC populations, leading to translation of the encoded influenza virus antigens of interest.

Biography

Pavlos C Englezou is a Post-doctoral Scientist in the Immunology Department at the Institute of Virology and Immunology in Mittelhäusern, Switzerland who has joined the group of Dr. Kenneth C. McCullough since 2013 and is working as part of the European UNIVAX consortium. He completed his PhD at the University of Manchester in the UK. His research interests lie in the development of novel vaccination strategies using nanotechnology. More specifically his work examines the capacity of cationic lipids to deliver self-replicating RNA to porcine dendritic cells as part of a new vaccination strategy against Influenza A viruses.

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