# Receptor mediated attachment of picornaviruses to liposomes and membrane translocation of genome RNA.

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## Introduction

Poliovirus is probably the best studied of the picornavirus family of non-enveloped RNA viruses. The structures of poliovirus, the poliovirus-receptor complex and cell-entry intermediate particles (the 135S and 80S particles), have all been well characterised. However, all this information is derived from molecules in free solution and the mechanism by which poliovirus enters cells remains poorly understood. We are therefore attempting to establish an *in vitro* system for structural, genetic and biochemical characterisation of early events in picornavirus infection in the context of model membranes. Preliminary studies have used poliovirus, future work will extend these techniques to study other picornaviruses, such as human rhinovirus, coxsackie viruses and foot-and-mouth disease virus.

## Preliminary results

Small unilamellar liposomes, generated using lipids with NTA-Ni head groups, were subsequently 'decorated' with soluble recombinant poliovirus receptor molecules containing a C-terminal $His_6$ tag. The presence of receptor allowed native poliovirus (160S) to bind to liposomes (Fig. 1). Receptor mediated conformational conversion to 135S and 80S subviral particles could subsequently be induced by incubation at 37°C. After removal of receptor molecules from liposomes by disruption of the NTA-Ni-$His_6$ interaction, converted particles remained membrane associated (Fig. 2), consistent with the prediction that hydrophobic viral sequences exposed during conversion are responsible for stable membrane anchoring.

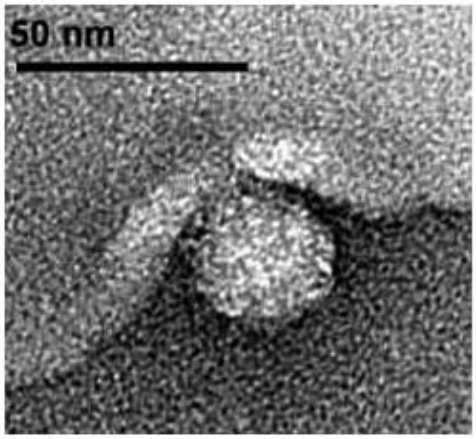


**Fig. 1** Poliovirus particle attached to poliovirus receptor bearing liposome

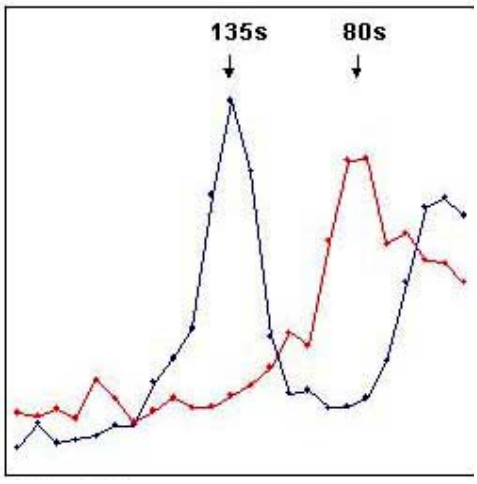


**Fig. 2** Sucrose gradient analysis showing conversion of polio virions to 135S particles on receptor bearing liposomes.

## Research in progress

Liposomes containing membrane impermeable dyes which fluoresce upon binding nucleic acid will enable us to detect translocation of viral RNA across the liposome membrane. Flow cytometry and FACS will be used to optimise the conditions required for these events. EM studies may provide novel structures of membrane associated particles.

## Collaborators

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