

# Secretory IgA directed to the inner core rotavirus VP6 protein contributes to protection via intracellular neutralization but not via immune exclusion

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Several IgA directed to the conserved inner core protein VP6 of rotavirus, such as the 7D9 mAb, can mediate protection. However these antibodies are not neutralizing in classical *in vitro* assays. As the IgA secretory pathway is involved in the protection of VP6 immune mice, we sought to determine the critical step of viral neutralisation in this pathway, i.e. either (1) at the mucosal surface by secretory IgA (SigA) or (2) intracellularly along the poly-Ig receptor transcytosis routing. No protection could be conferred by passively feeding mice with the anti-VP6 SigA 7D9 mAb, indicating that SigA 7D9 do not display classical immune exclusion properties *in vivo*. Interestingly, polymeric IgA (pIgA) 7D9, when applied at the basal pole of polarized CaCo2 or HT29 intestinal monolayers strongly reduced viral replication and prevented the loss of barrier function induced by rotavirus. Irrelevant pIgA and monomeric IgA 7D9 were inoperant. Thus pIgA can impede rotavirus replication by intersecting the VP6 protein in a key compartment where pIgA and VP6 interact. This finding highlights a mechanism by which the well conserved immunodominant VP6 protein induces heterotypic protection.

