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**Molecular events in production and transport of secretory IgA: a basis for design of reagents for passive immune protection.** JP Kraehenbuhl<sup>1</sup>, S Kerneis<sup>1</sup>, J Berdoz<sup>1</sup>, B Corthésy<sup>2</sup>, L Rindisbacher<sup>2</sup>, I Corthésy-Theulaz<sup>3</sup>, A Phalipon<sup>4</sup>, MR Neutra<sup>5</sup>, E Pringault<sup>1,6</sup> (<sup>1</sup> *Swiss Institute for Experimental Cancer Research and Institute of Biochemistry, University of Lausanne, 1066 Épalinges, Switzerland*; <sup>2</sup> *Institute of Animal Biology, University of Lausanne, 1015 Lausanne-Dorigny*; <sup>3</sup> *Division of Gastroenterology, Centre hospitalier universitaire vaudois, 1011 Lausanne, Switzerland*; <sup>4</sup> *Department of Molecular Pathogenicity, Institut Pasteur, Paris, France*; <sup>5</sup> *Childrens' Hospital and Harvard Medical School, Boston, MA, USA*; <sup>1,6</sup> *Institut Pasteur, unité des membranes, Paris, France*)

The major class of antibody produced by mucosal tissues lining the digestive, respiratory and urogenital tracts is secretory IgA (sIgA), made of 2 IgA monomers, one joining (J) chain and 1 or 2 molecules of secretory component (SC). Two cells cooperate to produce sIgA antibodies: the local plasma cells that secrete dimeric IgA and the epithelial cells that express the polymeric immunoglobulin (poly-Ig) receptor mediating transepithelial transport of the dimeric IgA. During transport, the receptor is cleaved and the SC that corresponds to the 5 receptors' Ig-like domains remains covalently bound to the IgA dimer providing resistance to proteolysis. In order to identify the mechanisms whereby sIgA antibodies protect mucosal surfaces, we have developed an *in vitro* system that mimics the *in situ* situa-

tion. Human or mouse intestinal epithelial cells that express the poly-Ig receptor were co-cultivated with hybridoma or myeloma cells that produce dimeric IgA antibodies. The monolayers were subsequently exposed to different pathogenic microorganisms, protective antibodies identified and the mechanisms of protection could then be analyzed. To facilitate the generation of monoclonal IgA antibodies, a novel strategy was designed for the isolation of the rearranged genomic variable heavy and light chain genes (Fv) of mouse immunoglobulin from hybridoma cell DNA. The amplified fragments are inserted into expression vectors containing mouse constant  $\alpha$  heavy- and light-chain DNA. The recombinant immunoglobulin DNA is then expressed in CHO or myeloma cells. In CHO cells IgA dimerization is obtained by J chain DNA co-transfection. Antibodies specific for *Clostridium difficile* toxin A and *Helicobacter pylori* urease have been generated by this procedure. *Shigella flexneri* liposaccharides were obtained by screening hybridoma cells for IgA producers. Our data indicate that IgA antibodies prevent microbial adhesion and/or invasion and that immune exclusion by pathogen crosslinking is not the only mechanism operating at mucosal cell surfaces. The system also allows us to analyze at which cell surface the antibodies exert protection and whether the IgA present in intracellular compartments plays a role.

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**Immunité lactogène et protection vaccinale dans l'espèce porcine.** H Salmon (INRA, laboratoire de pathologie infectieuse et immunologie, unité Lymphocyte et Immunité des muqueuses, 37380 Nouzilly, France)

## Introduction

Le porcelet nouveau-né, qui provient d'un milieu protégé (Berthon et Salmon, 1993), peut être brusquement confronté aux virus entéropathogènes, tel celui de la gastro-entérite transmissible (GET). Par transfert adoptif de porcelets nés de mères non immunes à des mères immunes (ayant présenté des signes de gastro-entérite lors de la gestation), Haelterman (1965) montra que les porcelets étaient protégés aussi longtemps qu'ils ingéraient le lait immun (et non le colostrum), d'où le terme d'immunité lactogène. Cette protection peut être repro-