

The vaxonella platform for oral recombinant vaccine delivery

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Vaxonella® achieves targeted mucosal delivery of plasmid-expressed vaccines via the lining of the small intestine. It uses the live attenuated *Salmonella enterica serovar Typhi strain ZH9* and associated genetic and formulation technologies. The ZH9 vector is very safe with attenuating mutations in genes for chrosimate synthase (*aroC*) and the type III secretion system (*ssaV*), and has been administered to over 400 volunteers in seven clinical trials (Phase I and II). It generates strong systemic and mucosal immune responses, making adjuvants unnecessary. Vaxonella features X-mark™, a technology that enables plasmids to be constructed using standard antibiotic selection in an Xer mutant strain of *E. coli*. These undergo automatic antibiotic resistance gene deletion by Xer recombination once transformed into any other enteric bacterium. The removal of the constitutively expressed selectable marker gene greatly reduces the major component of the metabolic burden which leads to plasmid loss. For further stability ORT-VAC™ is used: the only mechanism that enables maintenance of any enteric plasmid in the absence of an expressed selectable marker gene. A capsule formulation incorporating a bile-adsorbing resin protects dried *Salmonella* from the detrimental effects of bile until their natural resistance is restored by rehydration. Vaxonella® has been used to develop Typhetec®, a dual oral vaccine against typhoid and diarrhoea due to ETEC (Enterotoxigenic *Escherichia coli*). ETEC is the most common cause of diarrhoea amongst travellers yet there is no dedicated ETEC vaccine available. We are additionally developing a new oral vaccine against *Clostridium difficile*, a major cause of nosocomial infections.

Biography

Rocky M Cranenburgh is the CSO of Prokarium, a biotechnology company specialising in oral vaccine development and delivery. He completed a PhD in Genomics of Cyanobacteria at Newcastle University in 1997 and joined Cobra Biologics in Staffordshire later that year, a position which included a placement at the University of Oxford (1998-99). He led Cobra's Molecular Biology Group from 2000, which conducted numerous internal R&D projects and contracts for biopharmaceutical companies in the field of recombinant protein and DNA production. He was involved in spinning Prokarium out from Cobra in 2012, and has developed several new genetic technologies and vaccine candidates.

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