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## New approaches for the rational design of safer live attenuated bacterial vaccines

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**T**ypoid fever and non-typhoidal salmonellosis are responsible for a large disease burden worldwide and can coexist in the same geographical area.

Vaccination remains the most feasible means to counteract *Salmonella* infections. Live attenuated vaccines induce both antibody and protective Th1 responses that are essential to control bacteraemia during a secondary challenge and restrain growth and inter-organ spread of the bacteria in the systemic organs.

One of the concerns over the use of live vaccines is their potential residual virulence, especially in areas of the world where comorbidities and immunodeficiencies are prevalent and in many cases undiagnosed.

We have therefore searched for *Salmonella* genes that can be deleted to generate live attenuated vaccines with increased safety in situations where the immune system is impaired. We have used a global approach based on Transposon Directed Insertion-site Sequencing (TraDIS) to gain a numerical measure of the extent to which mutants are negatively or positively selected during infection in wild-type mice and in gene-targeted mice representative of common immunodeficiencies that predispose to salmonellosis. We have identified gene candidates that can be deleted to construct live vaccines with reduced and/or delayed reactogenicity in immunodeficient hosts. One of these vaccine strains has been further tested in immunocompromised mice and has shown increased safety as measured by delayed appearance of signs of infection in comparison with other established single mutant vaccine candidates. This mutant colonises mice via the oral and parenteral route and confers protection against lethal oral challenge with virulent *Salmonella*.

### Biography

Pietro Mastroeni received Degree in Medicine and Surgery from the University of Messina, Italy. He moved to the University of Cambridge, UK where he completed his Ph.D. before becoming a Research Fellow at Imperial College, University of London UK. He is currently a Reader in Infection and Immunity at the University of Cambridge. He has published more than 100 papers in reputed journals and served as an editorial board member.

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