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Christopher Chevillard

Axelle Amen

Solène Besson

Dalil Hannani

Isabelle Bally

See next page for additional authors

Authors

Christopher Chevillard, Axelle Amen, Solène Besson, Dalil Hannani, Isabelle Bally, Valentin Dettling, Salomé Gallet, Emilie Stermann, Guy Schoehn, Evelyne Gout, Daphna Fenel, Marlyse Buisson, Christophe Moreau, Pascal Poignard, Marie-Claire Dagher, and Pascal Fender

DEVELOPMENT OF AN INNOVATIVE ADENOVIRUS-INPIRED SELF-ASSEMBLING VACCINE PLATFORM RAPIDLY ADAPTABLE TO CORONAVIRUSES AND OTHER EMERGENT VIRUSES

Christopher Chevillard, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
christopher.chevillard@ibs.fr
Axelle Amen, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Solène Besson, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Dalil Hannani, UGA, CNRS, UMR 5525, VetAgro Sup, Grenoble INP, TIMC, 38000 Grenoble, France
Isabelle Bally, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Valentin Dettling, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Salomé Gallet, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Emilie Stermann, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Guy Schoehn, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Evelyne Gout, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Daphna Fenel, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Marlyse Buisson, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Christophe Moreau, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Pascal Poignard, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Marie-Claire Dagher, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France
Pascal Fender, CNRS, UGA, CEA, UMR5075, IBS, 38042 Grenoble, France

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The COVID-19 pandemic clearly shows how emergent diseases can cause severe global health and economic problems. We must be prepared to react swiftly against new pathogenic agents and this requires the development of vaccines that are safe, efficient in the long-term and easily adaptable with a short revision time. To this end, the COVID-19 mRNA and adenoviral vector vaccines have been spectacular successes, permitting rapid vaccination across the world in an unprecedented manner. Here we report the design of a new adenovirus-derived vaccine technology based on non-infectious pseudo-viral nanoparticles from the serotype 3 human adenovirus. Each nanoparticle comprises sixty identical proteins that assemble to form a 30 nm diameter spherical particle. A sequence has been engineered into the surface of this protein that enables the display of a covalently-bound target antigens. To demonstrate the efficiency of this approach, we added the SARS-CoV 2 spike protein receptor binding domain (RBD), that interacts with host cell ACE2 receptors, to the surface of the nanoparticles. We first showed that the glycosylated RBD retained its ACE2-binding function when displayed on nanoparticles. We then measured the *in vivo* humoral response of our vaccine candidate in mice and observed a strong antibody response after the prime injection; further levels were achieved following a second booster injection. In mice preimmunized with underivatized adenoviral nanoparticles, we tested if adenovirus seroprevalence, as frequently observed in humans, was detrimental to the RBD-mediated protection provided by our vaccine candidate. Interestingly, a strong anti-coronaviral response was still observed suggesting that existing circulating anti-adenovirus antibodies are not deleterious to our vaccine platform. We then performed pseudo-CoV 2 neutralization assays and obtained higher ID_{50} values than observed with COVID-19 convalescent sera, thus showing the high potential efficacy of our vaccine platform. This new vaccine technology is a tool that is easily adaptable to future SARS-CoV 2 variants and, more generally, to future emergent viruses and pathogens.