Annexes 2 à 5

Annexe 2 – Liste des publications – recherche vaccins SARS-CoV-2

Mise à jour 20200430

biorxiv	Insights into Cross-species Evolution of Novel Human Coronavirus 2019-nCoV and Defining Immune Determinants for Vaccine Development	https://doi.org/10.1101/2020.01.29.925867
biorxiv	The immune vulnerability landscape of the 2019 Novel Coronavirus, SARS- CoV-2	https://doi.org/10.1101/2020.02.08.939553
biorxiv	SARS-CoV-2 and SARS-CoV Spike-RBD Structure and Receptor Binding Comparison and Potential Implications on Neutralizing Antibody and Vaccine Devel	https://doi.org/10.1101/2020.02.16.951723
biorxiv	Crystal structure of Nsp15 endoribonuclease NendoU from SARS-CoV-2 Running Title: Structure of Nsp15 from SARS-CoV-2	https://doi.org/10.1101/2020.03.02.968388
biorxiv	In silico approach toward the identification of unique peptides from viral protein infection: Application to COVID-19	https://doi.org/10.1101/2020.03.08.980383
biorxiv	Development of CRISPR as a prophylactic strategy to combat novel coronavirus and influenza	https://doi.org/10.1101/2020.03.13.991307
biorxiv	A Cryptic Site of Vulnerability on the Receptor Binding Domain of the SARS-CoV-2 Spike Glycoprotein	https://doi.org/10.1101/2020.03.15.992883

biorxiv	COVID-19 coronavirus vaccine design using reverse vaccinology and machine 1 learning 2 3	https://doi.org/10.1101/2020.03.20.000141
biorxiv	Emergence of SARS-CoV-2 through Recombination and Strong Purifying Selection Short Title: Recombination and origin of SARS-CoV-2 One Sentence Sum	https://doi.org/10.1101/2020.03.20.000885
medrxiv	The local stability of a modified multi-strain SIR model for emerging viral strains	https://doi.org/10.1101/2020.03.19.20039198
biorxiv	Using directed attenuation to enhance vaccine immunity	https://doi.org/10.1101/2020.03.22.002188
biorxiv	Analysis of Serologic Cross-Reactivity Between Common Human Coronaviruses and SARS-CoV-2 Using Coronavirus Antigen Microarray	https://doi.org/10.1101/2020.03.24.006544
biorxiv	Structure-based modeling of SARS-CoV-2 peptide/HLA-A02 antigens 1 2 Materials and Methods Identification of SARS-CoV-2 peptide epitopes	https://doi.org/10.1101/2020.03.23.004176
biorxiv	SARS-CoV-2 exhibits intra-host genomic plasticity and low-frequency polymorphic quasispecies	https://doi.org/10.1101/2020.03.27.009480
biorxiv	Site-specific analysis of the SARS-CoV-2 glycan shield	https://doi.org/10.1101/2020.03.26.010322
biorxiv	Potent neutralizing antibodies in the sera of convalescent COVID-19 patients 1 are directed against conserved linear epitopes on the SARS-CoV-2 s	https://doi.org/10.1101/2020.03.30.015461
biorxiv	Sequence analysis of SARS-CoV-2 genome reveals features important for vaccine design	https://doi.org/10.1101/2020.03.30.016832
Elsevier	Novel decoy cellular vaccine strategy utilizing transgenic antigen-expressing cells as immune presenter and adjuvant in vaccine prototype against	https://doi.org/10.1016/j.medidd.2020.100026
biorxiv	Prediction of SARS-CoV-2 epitopes across 9360 HLA class I alleles	https://doi.org/10.1101/2020.03.30.016931
Elsevier	Microneedle array delivered recombinant coronavirus vaccines: Immunogenicity and rapid translational development	https://doi.org/10.1016/j.ebiom.2020.102743
biorxiv	A SARS-CoV-2 Vaccination Strategy Focused on Population-Scale Immunity	https://doi.org/10.1101/2020.03.31.018978
biorxiv	Leveraging mRNAs sequences to express SARS-CoV-2 antigens in vivo	https://doi.org/10.1101/2020.04.01.019877
medrxiv	Differential COVID-19-attributable mortality and BCG vaccine use in countries	https://doi.org/10.1101/2020.04.01.20049478
medrxiv	Face mask use in the general population and optimal resource allocation during the COVID-19 pandemic	https://doi.org/10.1101/2020.04.04.20052696
PMC	Single-Dose, Intranasal Immunization with Recombinant Parainfluenza Virus 5 Expressing Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Sp	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC715777
PMC	Better Epitope Discovery, Precision Immune Engineering, and Accelerated Vaccine Design Using Immunoinformatics Tools	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC715410
biorxiv	Title Sequence-based prediction of vaccine targets for inducing T cell responses to SARS-CoV-2 2 utilizing the bioinformatics predictor RECON 3	https://doi.org/10.1101/2020.04.06.027805
biorxiv	Immunoglobulin fragment F(ab') 2 against RBD potently neutralizes SARS-CoV-2 in vitro	https://doi.org/10.1101/2020.04.07.029884

biorxiv	The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) envelope (E) protein harbors a conserved BH3-like sequence	https://doi.org/10.1101/2020.04.09.033522
biorxiv	Rapid in silico design of antibodies targeting SARS-CoV-2 using machine learning and supercomputing 1	https://doi.org/10.1101/2020.04.03.024885
Elsevier	Journal Pre-proof COVID-19 Coronavirus spike protein analysis for synthetic vaccines, a peptidomimetic antagonist, and therapeutic drugs, and ana	https://doi.org/10.1016/j.compbiomed.2020.103749
medrxiv	Exercising caution in correlating COVID-19 incidence and mortality rates with BCG vaccination policies due to variable rates of SARS CoV-2 testin	https://doi.org/10.1101/2020.04.08.20056051
biorxiv	A single dose of ChAdOx1 MERS provides broad protective immunity against a variety of MERS-CoV strains	https://doi.org/10.1101/2020.04.13.036293
medrxiv	Sequential Vaccination for Containing Epidemics	https://doi.org/10.1101/2020.04.13.20060269
PMC	Repurposing Didanosine as a Potential Treatment for COVID- 19 Using Single-Cell RNA Sequencing Data	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC71599
medrxiv	Molecular mechanism of action of repurposed drugs and traditional Chinese medicine used for the treatment of patients infected with COVID-19: A s	https://doi.org/10.1101/2020.04.10.20060376
medrxiv	Bayesian Adaptive Clinical Trials for Anti-Infective Therapeutics during Epidemic Outbreaks *	https://doi.org/10.1101/2020.04.09.20059634
biorxiv	TMPRSS2 and furin are both essential for proteolytic activation and spread of SARS- 1 CoV-2 in human airway epithelial cells and provide promisin	https://doi.org/10.1101/2020.04.15.042085
biorxiv	A Large-scale Drug Repositioning Survey for SARS-CoV-2 Antivirals	https://doi.org/10.1101/2020.04.16.044016
Elsevier	Journal Pre-proof The Potential Role of Th17 Immune Responses in Coronavirus Immunopathology and Vaccine-induced Immune Enhancement The Potential	https://doi.org/10.1016/j.micinf.2020.04.005
biorxiv	Structure-based design of hepatitis C virus E2 glycoprotein improves serum binding and cross-neutralization	https://doi.org/10.1101/2020.04.15.044073
Elsevier	Journal Pre-proof Innovations in structure-based antigen design and immune monitoring for next generation vaccines Title: Innovations in structur	https://doi.org/10.1016/j.coi.2020.03.013
Elsevier	Nanoparticle-based vaccines: opportunities and limitations	https://doi.org/10.1016/b978-0-12-817778-5.00007-5
Elsevier	Harnessing γδ T Cells as Natural Immune Modulators	https://doi.org/10.1016/b978-0-12-811924-2.00046-8

Annexe 3 – National Vaccine Plan

Date de 2010.

Octobre 2019 lancement d'une « *request for information* » par le *Office of Infectious Disease and HIV/AIDS Policy*, destiné à sollicitant les **commentaires des parties prenantes sur les priorités, les buts et les objectifs potentiels du nouveau plan national de vaccination 2020**.

Priorités :

- Adult Immunization
- HPV Vaccination
- Vaccine Confidence
- Vaccine Innovation
- Vaccine Safety

Plan / Objectives

Goal 1: Develop New and Improved Vaccines

- Prioritize new vaccine targets of domestic and global public health importance.
- Support research to develop and manufacture new vaccine candidates and improve current vaccines to prevent infectious diseases.
- Support research on novel and improved vaccine delivery methods.
- Increase understanding of the host immune system.
- Support product development, evaluation, and production techniques of vaccine candidates and the scientific tools needed for their evaluation.
- Improve the tools, standards, and approaches to assess the safety, efficacy, and quality of vaccines.

Goal 2: Enhance the Vaccine Safety System

- Ensure a robust vaccine safety scientific system that focuses on high priority areas.
- Facilitate the timely integration of advances in manufacturing sciences and regulatory approaches relevant to manufacturing, inspection, and oversight to enhance product quality and patient safety.
- Enhance timely detection and verification of vaccine safety signals.
- Improve timeliness of the evaluation of vaccine safety signals, especially when 1) a high-priority new vaccine safety concern emerges or 2) when a new vaccine is recommended, vaccination recommendations are expanded, or during public health emergencies such as in an influenza pandemic or other mass vaccination campaign.
- Improve causality assessments of vaccines and related AEFIs.
- Improve scientific knowledge about why and among whom vaccine adverse reactions occur.
- Improve clinical practice to prevent, identify and manage vaccine adverse reactions.
- Enhance collaboration of vaccine safety activities.

Goal 3: Support Communications to Enhance Informed Vaccine Decision making

- Utilize communication approaches that are based on ongoing research.
- Build and enhance collaborations and partnerships for communication efforts.
- Enhance delivery of timely, accurate, and transparent information to public audiences and key intermediaries (such as media, providers, and public health officials) about what is known and unknown about the benefits and risks of vaccines.

- Increase public awareness of the benefits and risks of vaccines and immunization, especially among populations at risk of under-immunization.
- Assure that key decision- and policy makers (e.g., third-party payers, employers, legislators, community leaders, hospital administrators, health departments) receive accurate and timely information on vaccine benefits and risks; economics; and public and stakeholder knowledge, attitudes, and beliefs.

Goal 4: Ensure a Stable Supply of, Access to, & Better Use of Recommended Vaccines in the United States

- Ensure consistent and adequate supply of vaccines for the United States.
- Ensure consistent and stable delivery of vaccines for the United States.
- Reduce financial barriers to vaccination.
- Maintain and enhance the capacity to monitor immunization coverage for vaccines routinely administered to all age groups.
- Enhance tracking of VPDs and monitoring of the effectiveness of licensed vaccines.
- Educate and support health care providers in vaccination counseling and vaccine delivery for their patients and themselves.
- Maintain a strong, science-based, transparent process for developing and evaluating immunization recommendations.
- Strengthen the National Vaccine Injury Compensation Program (VICP) and Countermeasures Injury Compensation Program (CICP).
- Enhance immunization coverage for travelers.

Goal 5: Increase Global Prevention of Death & Disease through Safe & Effective Vaccination

- Support international organizations and countries to improve global surveillance for VPDs and strengthen health information systems to monitor vaccine coverage, effectiveness, and safety
- Support international organizations and countries to improve and sustain immunization programs as a component of health care delivery systems and promote opportunities to link immunization delivery with other priority health interventions, where appropriate.
- Support international organizations and countries to introduce and make available new and underutilized vaccines to prevent diseases of public health importance.
- Support international organizations and countries to improve communication of evidence-based and culturally and linguistically appropriate information about the benefits and risks of vaccines to the public, providers, and policy-makers.
- Support the development of regulatory environments and manufacturing capabilities that facilitate access to safe and effective vaccines in all countries.
- Build and strengthen multilateral and bilateral partnerships and other collaborative efforts to support global immunization and eradication programs.

Annexe 4. Détails des financements votés par le congrès

Coronavirus Preparedness and Response Supplemental Appropriations Act - signé le 6 mars 2020, pour première intervention d’urgence : enveloppe totale de $8,7 milliards dont

$2 milliards à la BARDA pour la recherche et le **développement de vaccins**, de produits thérapeutiques et de diagnostics.

- $836 millions au *National Institute of Allergy and Infectious Diseases* du NIH afin de mener des recherches sur les thérapies, **les vaccins,** les diagnostics et d'autres technologies de la santé.
- $61 millions à la *Food and Drug Administration* (FDA) : pour le développement et **l'examen des candidats vaccins**, des produits thérapeutiques, des dispositifs médicaux, le déploiement opérationnel pour garantir la sécurité de la chaîne d'approvisionnement et le soutien à la lutte contre les produits contrefaits.

Coronavirus Aid, Relief, and Economic Security (CARES) Act - signé le 25 mars 2020

Le plan de soutien massif d’un budget total estimé à plus de $2,000 milliards voté ce mercredi 25 juin prévoit un financement de $415 millions alloués au Department of Defense (DoD) pour le développement de **vaccins** et antiviraux, des tests en laboratoire ainsi que l’achat de tests pour la détection du COVID-19. Le “ Take Responsibility for Workers and Families Act précise les approvisionnements déjà fournis par le CARES Act ou en préparation des futurs plans de réponse à la pandémie, qui sont en cours d’élaboration :

- $945 millions au *National Institutes of Health* (recherche sur les vaccins, la recherche thérapeutique ainsi que les diagnostics du COVID-19 et les risques cardiovasculaires et pulmonaires sous-jacents)
- $76 millions pour la *National Science Foundation* (continuité des programmes de recherche en cours sur le COVID-19)
- $99.5 millions pour L’*Office for Science du Department of Energy* (continuité des activités de recherche dont les priorités ont été dirigées vers le COVID-19)
- $945 millions au National Institutes of Health : pour la.

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Annexe 5 – ACTIV, Les partenaires

Actions prioritaires d'ACTIV dans le domaine des vaccins :

Faire avancer le développement de vaccins par :

- En créant un cadre de collaboration pour partager les connaissances sur l'immunité naturelle et la réponse immunitaire induite par les candidats vaccins par :
  - Cartographie des épitopes et développement de tests
  - Établissement de protocoles pour l'échantillonnage, les analyses immunologiques et les réactifs
  - Collecte de données cliniques sur les réponses immunologiques et les critères de jugement, afin de permettre une méta-analyse des corrélations sur la protection
  - S'engager avec les régulateurs sur des critères de substitution pour l'évaluation clinique

Liste des participants au consortium ACTIV (https://www.nih.gov/news-events/news-releases/nih-launch-public-private-partnership-speed-covid-19-vaccine-treatment-options), dernière mise à jour le 17 avril 2020.

<u>Government</u>

- National Institutes of Health
- HHS Office of the Assistant Secretary for Preparedness and Response
- U.S. Food and Drug Administration
- Centers for Disease Control and Prevention
- European Medicines Agency

<u>Non-Profit</u>

- Foundation for the National Institutes of Health

<u>Industry</u>

- AbbVie
- Amgen
- AstraZeneca
- Bristol Myers Squibb
- Evotec
- GlaxoSmithKline
- Johnson & Johnson
- KSQ Therapeutics
- Eli Lilly and Company
- Merck & Co., Inc.
- Novartis
- Pfizer
- Roche
- Sanofi
- Takeda
- Vir Biotechnology