Ingediende voorstellen ZonMw programma second wave corona, mei 2020

Projectvoorstellen met het CIb als hoofdaanvrager:

#	Indiener (centrum + naam)	titel	ZonMW abstract van 2000 karakters	Partners binnen RIVM	Partners buiten RIVM
1	Dr. (10)(2e), (10)(2e) (Main applicant) IDS	The role of prior exposure to livestock-associated coronaviruses in severity of COVID-19 through antibodydependent enhancement (ADE)	The current SARS-CoV-2 pandemic demonstrates large discrepancies in incidence of severe disease depending on geographic distribution and age. A possible biological explanation might be that individuals suffering the most have been primed by one or more prior coronavirus exposures, are experiencing the effects of antibody dependent enhancement (ADE) of viral infection. This phenomenon has been demonstrated and characterized for SARS-CoV and postulated for SARS-CoV-2. By comparing maps of livestock density in The Netherlands with maps depicting hospitalized COVID-19 patients striking patterns can be observed, which are supported by preliminary data from spatial analyses, indicating that severe disease occurs more in patients living in close proximity to certain livestock farms. We hypothesize that livestock-associated coronaviruses are priming viruses that induce antibodies in humans, putatively mediating ADE of SARS-CoV-2 and subsequently enhancing infection and severity of disease. To test our hypothesis the following research questions will be addressed: I. Does (part of) the Dutch population have antibodies to animal coronaviruses? II. Do these antibodies to animal coronaviruses cross-react with and mediate ADE of SARS-CoV-2 in vitro? III. Is presence of these antibodies to animal coronaviruses related to severity of COVID-19 disease? IV. Is anti-animal-CoV seroprevalence in humans associated with the regional distribution of severe COVID-19 cases? If prior exposure to animal coronaviruses indeed has an effect on COVID-19 this would have important implications for identification of risk groups with regards to mitigation and exit strategies as well as vaccine safety. Moreover, closer monitoring of patients with potential ADE-inducing antibodies and development of	(10)(2e) (10)(2e) (10)(2e) (10)(2e) (10)(2e)	(10)(2e) (10)(2e) (10)(2e) (10)(2e)

			specific treatment regimens may improve clinical outcome.		
2	(10)(2e) (10)(2e) (IDS)	Fecal excretion of infectious SARS-CoV-2 particles (Fexcretion)	Although human coronaviruses are primarily considered as respiratory pathogens, tropism for the gastrointestinal tract, with fecal-oral transmission as alternative route for infection, has been described for all of them. Here, we propose to support an evidence-based mitigation of risks for SARS-CoV-2 transmission in clinical and public health settings by studying the possible role of gastrointestinal shedding of SARS-CoV-2 by children and adults. To this goal we aim to: - study the level of infectivity of SARS-CoV-2 in stool samples in relation to severity of clinical manifestation, age, timing of sampling and level of genomic RNA detection. - study possible age-dependent differences in respiratory and gastrointestinal tissue tropism between children and adults. -gain insight in the source of observed high level and frequent detection of SARS-CoV-2 in wastewaters. -determine and characterize presence of evolutionary pressure towards emergence of SARS-CoV-2 strains with increased fecal –oral transmission potential and/or increased transmission among children. The data collected in this study will direct guidelines aimed at prevention of fecal-oral transmission of SARS-CoV-2 in clinical and Public Health settings, e.g. laboratories, hospitals, nursing homes, day care centres and schools.	(10)(2e) (10)(2e) (10)(2e) (10)(2e) (10)(2e) (10)(2e) (10)(2e) (10)(2e) (10)(2e)	(10)(2e) (10)(2e) (10)(2e) (10)(2e)

Projectvoorstellen met een andere partij als hoofdaanvrager en het CIb als partner:

#	Indiener (naam + organisatie)	Tit
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#	Indiener (naam + organisatie)	Titel	ZonMW Abstract 2000 woorden	Partners binnen RIVM	Partners buiten RIVM
1	(10)(2e)	**SARSLIVA:** utility of saliva in diagnosis, detecting co-infections, and evaluating household transmission in COVID-19	Saliva is an obvious source for SARS-CoV-2 detection. The virus's ability to infect and actively reproduce in the upper respiratory tract was shown last month by Wendtner et al, who reported on experiments that virus from the throats of nine people with COVID-19 could be cultured, showing that the virus is actively reproducing and infectious there. Saliva gland ducts also express the ACE2 receptor for the virus in rhesus macaques. High viral loads were already present in the saliva of COVID-19 patients at the onset of disease, which could account for the fast-spreading nature of this epidemic. Also, SARS-CoV-2 infection appears to shed viral particles from the throat into saliva even before symptoms start. Pre-symptomatic transmission was estimated to contribute to up to 60% of COVID-19 cases in China. Saliva may therefore be the obvious tool to detect a-symptomatic and pre-symptomatic individuals before actual symptoms present. When saliva proves to detect low viral loads, COVID-19 patients, who may remain symptomatic for weeks to months, can be followed to see whether they still spread the virus. To validate saliva for these purposes, we propose a study where we 1. Follow confirmed COVID-19 patients with home self -	**RIVM:** -The viral diagnostic unit Dr (10)(2e) (10)(2e), Dr (10)(2e) (10)(2e), (10)(2e) - Dr (10)(2e) (10)(2e), (10)(2e) - Dr (10)(2e) (10)(2e)	**UMCU &RIVM:** Molecular diagnostics (bacterial); dr (10)(2e) (10)(2e), collaborating with RIVM. Long standing experience with saliva as specimen for tracing bacterial infections. **UMCU WKZ & RIVM:** (10)(2e) (10)(2e), (10)(2e) and currently also (10)(2e) experienced in large scale trials on respiratory infections and

				sampling of saliva for 4-6 weeks and at least two weeks after symptoms have stopped. 2. Follow household members for 4-6 weeks to detect potentially pre-symptomatic and a-symptomatic SARS-CoV-2 infected individuals. 3. Follow emerging IgA and IgG anti-SARS-COV-2 antibodies in saliva over time 4. Detect other respiratory viruses present in relation to symptoms of infection. The study is a close collaboration between the Spaarne hospital, Streeklaboratorium Haarlem, and the RIVM where viral diagnostics will be performed and mucosal SARS-CoV-2 antibody emergence. If we can use saliva for early detection, and at low viral loads in the course of infection, containment of viral spread is made easier and allows for improved policies in this pandemic.		microbiome studies. **Streeklab Haarlem:** Dr. (10)(2e) (10)(2e) Haarlem, Dr. (10)(2e) (10)(2e) epidemiologist **Spaarne Gasthuis:** Dr. (10)(2e) (10)(2e) and Dr. (10)(2e)
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