CoV2K Effects Taxonomy

This document overviews the taxonomy used in CoV2K for categorizing the effects of single amino acid changes, groups of amino acid changes, and variants of SARS-CoV-2.

The taxonomy is composed of four main categories, described in the following.

Category 1: Epidemiology

This category classifies the impact of a change, a group of changes, and/or a variant on epidemiological features, namely:

a. Viral transmission (`viral_transmission`): The virus capability to pass from one host to another host [1].
b. Infectivity: The capability of a transmitted virus to establish an infection [2].
c. Viral virulence (`viral_virulence`): The competence of any infectious agent to produce pathologic effects [3].
d. Disease severity (`disease_severity`): An assessment of systematic symptoms caused by the virus [4].
e. Risk of hospitalization (`risk_of_hospitalization`): The risk of placing a patient in a hospital for diagnostic study and/or treatment [5]. Severe episodes of illness can require hospitalization and be an indicator that routine treatment in outpatient settings is not being delivered effectively to the whole population [2].
f. Risk of re-infection (`risk_of_reinfection`): The risk of a second infection by the same infectious agent, after recovery from – or during the course of – a primary infection.
g. Fatality rate (`fatality_rate`): The proportion of people who die after the viral infection over the number of confirmed infected people [2].
h. Complication with other diseases (`complication_with_other_diseases`): a concurrent disease, accident, or adverse reaction that aggravates the original disease.

Category 2: Immunology

This category classifies the impact of a change, a group of changes, and/or a variant on the host immune system; therefore, it captures effects related to the interaction between the infectious agent and any host immune elements. This category is important for the development of vaccines and treatments:

a. Sensitivity to neutralizing mAbs (`sensitivity_to_mAbs`): It measures the sensitivity of the variants towards monoclonal antibodies – the mechanism by means of which a subset of antibodies blocks the viral infection is called neutralization. This kind of sensitivity has a crucial role in vaccine development [6].
b. Sensitivity to convalescent sera (`sensitivity_to_convalescent_sera`): It measures the sensitivity towards the convalescent serum from recovered individuals. As in other infections, the convalescent serum might be used for prevention and treatment of COVID-19, as it is assumed that convalescent plasma donors may have developed an effective immune response to the offending pathogen [7].

c. Sensitivity to vaccinated sera (`sensitivity_to_vaccine_sera`): It measures the sensitivity towards the convalescent serum from vaccinated individuals. This serum is relevant as it is assumed that vaccinated plasma donors may have developed an effective immune response to the offending pathogen.

Category 3: Viral kinetics and dynamics

This category classifies the impact of a change, a group of changes, and/or a variant on the kinetics or dynamics of viral proteins and the cell cycle, which has an important impact on the way of dealing with the virus.

a. Protein flexibility (`protein_flexibility`): Proteins are dynamic entities, and they possess an inherent flexibility that allows them to function through molecular interactions [8]. Proteins rely on flexibility to respond to environmental change, potentially, a perturbation that changes the flexibility of a protein may interfere with its function [9].
b. Protein stability (`protein_stability`): Stability is the potential of a pattern to survive over time, and therefore is integral to our understanding of biological systems and their evolution [10]. Since proteins are dynamic entities, they need to possess a specific level of stability to survive and perform their functions [11].
c. Intraviral protein-protein interactions (`intraviral_protein_protein_interaction`): The function and activity of a protein are often modulated by other proteins with which it interacts [12].
d. Binding to host receptor (`binding_to_host_receptor`): SARS-CoV-2 enters the host cells by binding its receptor-binding domain (RBD), in the Spike protein, to a cell receptor called angiotensin-converting enzyme 2 (ACE2). Modifying the binding affinity could lead to a change in the efficacy of cell entering. Hence, binding affinity potentially affects cell infectivity and immune evasion [13].
e. Binding to antibodies (`binding_to_Abs`): Antibodies are key tools to fight against SARS-CoV-2 both in the treatment and prevention domains; therefore, studying the binding affinity and activity of a protein to antibodies is relevant for attempting to neutralize antibody response [14].
f. Viral load (`viral_load`): It measures the number of copies of RNA of a given virus per milliliter of blood [15].

Category 4: Diagnosis, prevention, and treatments

a. Effectiveness of available diagnostics (`effectiveness_of_available_diagnostics`): Three methods are used to diagnose SARS-CoV-2 infection, i.e., PCR tests, antibody tests, and antigen tests. Given mutations may impact the diagnostic sensitivity of these methods [16].
a. Effectiveness of available vaccines (`effectiveness_of_available_vaccines`): Newly emerging mutations and variants may affect the protective efficacy of an existent designed vaccine [17].
b. Effectiveness of available antiviral drugs (`effectiveness_of_available_antiviral_drugs`): Some mutations may impact the effectiveness of an antiviral drugs. This impact may range from slightly modifying the effectiveness of specific therapy till completely becoming resistant to that therapy [18].

Methods:

The information concerning the effect of a change, a group of changes, and/or a variant, is also (tentatively) connected to one of four methods describing the methodology used in the source research study reporting the result. Those methods are:

1. Epidemiological: The experiment is performed on a target group of people (or on viral sequences) with a set of metadata.
2. Experimental: The experiment is performed in laboratories (in vitro and in vivo).
3. Computational: The effect is computed as a result of specific computational analysis.
4. Inferred: The effect of a change is inferred as a consequence of the effect produced by another change (revealed with a different analysis/study).

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