Glutathione pathway and GST polymorphisms in the immune response to SARS-CoV-2: The missing piece of the COVID-19 puzzle

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The pandemic of COVID-19 disease, a respiratory condition caused by a novel coronavirus (SARS-CoV-2) in December 2019, has been evidently effectively controlled by vaccines. As of 31st May 2021, there are 170,189,835 confirmed cases in over 240 countries with over 3,538,196 deaths. It is characterized by a myriad of both respiratory and non-respiratory symptoms. Most individuals with the infection will have mild symptoms that are naturally resolved by an active immune system. However, a subset of people with a higher risk of infection is the elderly and those with comorbidities such as heart disease, diabetes, asthma, and cancer. The human immune response against viral infection is mainly dependent on active T cell function. Glutathione (GSH), a ubiquitous tri-peptide antioxidant known for homeostasis regulation and important in oxidative stress response, is essential for T cell effector functions through its regulation of metabolic activity.

Glutamyl cysteine ligase (GCL) catalyses the rate-limiting step of glutathione synthesis. Polymorphisms in this enzyme impede glutathione synthesis. Glutathione S-transferases (GSTs) catalyse the conjugation of glutathione to xenobiotic, reactive oxygen species (ROS), toxins, and other cellular by-products. Alterations in the structure, function, or level of expression of GST genes could alter the ability of the cell to inactivate toxins, thereby aggravating the progression of infection. GST polymorphisms have been clearly associated with such comorbidities including various cancers and respiratory diseases. It is well known that oxidative stress is a major factor in the pathogenesis of viral respiratory infections. Evidently, full dosed individual is still susceptible to infection and severe illness from the virus with possible hospitalization. Recovery from infection is associated with traumatic pain and fatigue, breathlessness, and negatively impacted morbidity. It is therefore possible that GST polymorphisms may impair immune response against the coronavirus. To the best of our knowledge, the potential implications of GCLC & GST gene polymorphisms on SARS-CoV-2 infection have not been elucidated.

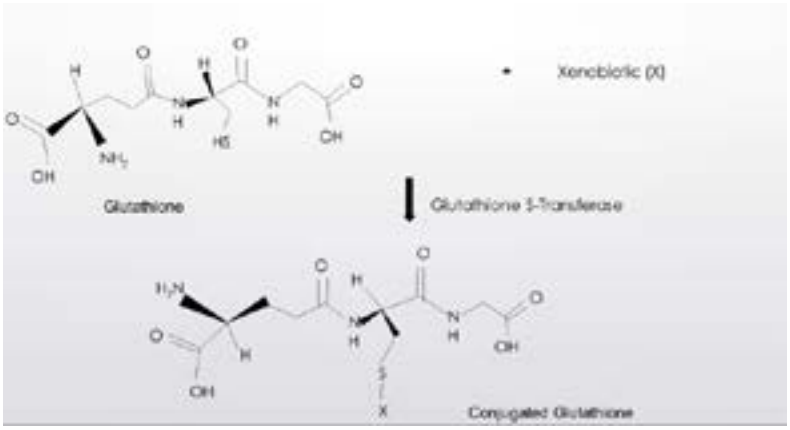

Figure: The Schematic Diagram of Function of glutathione

Biography

Bene A. Ekine-Afolabi is a graduate of River State University of Science & Technology in Applied Biology (Medical Microbiology option); with an MRes degree at University of East London, United Kingdom. She had her PhD study & worked at the Department of Natural Sciences, Middlesex University, UK. Trained in practical approach to toxicology in drug development (American College of Toxicology/British Toxicology Society). Bene does research in Microbiology, Molecular Biology and Cancer: Her current focus of research (which has yielded eight designed models), is on the Investigation of molecular mechanism of colorectal cancer and due to the current pandemic, has been involved in drug development for COVID-19. Bene had Harvard University part-sponsored training in therapeutic research in Cancer Biology & Therapeutic.