We, humans, are very diverse—tall, short, dark, fair—there are so many traits we are born with! One can trace this diversity to our genes, which are shaped over time, to reach their present form. However, did you know your genes can also have a say in how susceptible you are to an infection caused by a particular strain of virus? In a recent study (https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1006069), researchers from India and the UK have studied the role of the genes that control our immune response and how they play a crucial role in countering the spread of H1N1 influenza. The study was led by Prof. Nagasuma Chandra from the Indian Institute of Science (IISc), Bengaluru and Prof. Gautam Menon from the Institute of Mathematical Sciences (IMSc), Chennai, in collaboration with Prof. Carmen Molina-París and Dr. Martín López-García from the University of Leeds, UK.

In 2009, the world was hit by the H1N1 swine flu pandemic, which is believed to have originated from three sources—birds, pigs, and humans. The human flu viruses further combined with the Eurasian pig flu viruses, devastating the situation. The first step in containing the infection was to understand the genetic makeup of the causative virus. Researchers all over the world shared the genetic sequences of the virus within days of identification, and the data was available for different countries, which comprised of multiple ethnicities.

However, not all exposed to the influenza virus end up being infected. As Prof. Gautam Menon from IMSc and a co-author of the study says "You and I might have identical exposure to a novel virus, yet you might fall ill, and I might stay uninfected." So, then what contributes to the susceptibility of an individual and what controls how the virus spreads in a population? Turns out, it is the immune response and its diversity due to variations in the genes!

> *"We estimate the susceptibility of an individual to a strain of H1N1 influenza by focusing on a specific immune molecule called human leukocyte antigen class - I (HLA class-I). This is an important player in recognising the presence of a foreign body such as a virus", says Prof. Chandra. Fragments of the virus which are recognised by the immune system are called epitopes. The more the number of epitopes, the less susceptible the individual is to the infection.*

The researchers, with Ms Narmada Sambaturu of IISc as the first author of the study, used a mathematical model, called the SIR (Susceptible - Infected - Recovered) model, to study how the presence of susceptibility in sub-populations affects the spread of the disease. They started by dividing the population into subpopulations based on their vulnerability to the infection. As per the model, initially, the individuals are susceptible but not infected. Gradually when a virus is

introduced, the individuals become infected at a rate determined by their estimated susceptibility to the pathogen, which is calculated using the genetic information about the host and the pathogen. At a later stage, these infected individuals proceed to recovery.

The findings reveal that if the population diversity is higher, it is less likely that the infection will spread. “A central result of our work is that genetic diversity can act as a protective barrier against disease spread", says Prof. Chandra. Therefore, understanding an individual's susceptibility to a virus, as well as the different levels of vulnerability in a population, are key to containing the spread of infection. Knowing who the super-spreaders are and which individuals are highly susceptible can ultimately help policymakers decide whom to vaccinate or who should be quarantined and how to allocate resources to maximise impact.

The researchers of the current study have used data of individuals from 61 ethnicities, and of 81 viral strains isolated in 2009, as well as 85 viral strains isolated in other years. “Unfortunately, there is no systematic data about genetic makeup relevant to our models that covers Indian populations”, says Prof. Menon. The findings of the study are published in the journal *PLOS Computational Biology*, and the research was supported by fellowships from the Department of Science and Technology and the European Commission.

As a next step, the researchers stress the need for publicly available information for the Indian population. "We’re trying to see whether we can arrange to collect the data required to capture immunological features of the Indian population. This effort will involve substantial work, but the payoff should come from better understanding how infectious diseases spread in India and better planning for epidemics”, say Prof. Chandra and Prof. Menon.

Tags: IISc (/iisc) DBT (/tags/dbt) H1N1 (/tags/h1n1) Swine flu (/tags/swine-flu) Influenza (/tags/influenza) genetics (/tags/genetics)