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Immunity: A Mensa IQ, An Elo rating, Van Gogh Temperaments, Chain Reactions, but A Treasure Trove

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1. Immunity: At a Glance

Immunity is how organisms from prokaryotes to archaea, choanoflagellates to humans, green algae to angiosperms, all stay guarded against the perpetually sinister presence of intruders who come in a multitude of forms, especially as pathogenic viruses threatening humans, plants, and bacteria alike. Immunity has a high IQ, is a tactician like a grand master in a game of immunological chess, primes chain reactions using signal cascades, and sometimes self-destructs like a certain Dutch artist of yesteryear, to prevent a more potent and widespread infection outcome.

2. Human Immunity: Protein Personalities

Human immunity is a multi-prong, many layered cascades of myriad of events that eliminates challenges imposed by hazardous and malignant intruders, which can provide morbidity outcomes as well as result in unexpected fatalities. Immunity, at the first stage, can be termed as native or innate, forming the first line of defense that is rarely specific or streamlined and largely a blunt form of rescue. Adaptive immunity, which is stimulated by primary, secondary, or tertiary structures of macromolecules termed as epitopes, is a strict reaction elicited to eliminate or attenuate the dangers of an invading organism like a virus, following foreign antigen presentation triggering humoral or cell-mediated immunity. While immunity in plants, bacteria and humans share some of the same elements, there are striking differences between the three offshoots of evolution, and such distinctions can shed more light on how we – scientists – can ensure that immunity be finetuned and tailored for beneficial outcomes while not harming the host impacted by the operational landscape of virulence.

3. Plant Immunity: roots, shoots, and cahoots

Plant immunity can be polygonal with defensive walls such as callose deposition and strengthening of cell walls, cell death such as in the hypersensitive reaction, phytoalexins and other pathogen perforating molecules, pattern recognition receptors that are able to distinguish pathogens inducing local responses and Systemic Acquired Resistance [SAR], a mechanism which snowballs from a local infection into a signaling avalanche, taking into account the non-self-molecules to protect the plant from potentially harmful consequences.

4. Bacterial Immunity: Immune Ecosystems

While bacterial immunity has been largely bolstered by the multi depth exploration of how *Streptococcus pyogenes* retaliates to bacteriophage infection and the resulting Nobel-prize winning and game-changing innovation of CRISPR-Cas technologies [Clustered Regularly Interspaced Short Palindromic Repeats] that have taken the molecular landscape by storm, providing toolboxes of molecular scissors that can break open nucleic acid backbones by reading specific barcodes belonging to foreign pathogens and has innovated by the breakthrough of the "genome editing" industry, where we have a potential solution to harmful mutations [Cystic Fibrosis, Thalassemia etc] that pay a toll as monogenic diseases [1]. Such developments have

resulted in the shifting of paradigms of gene therapy - where a corrective gene is introduced packaged in vectors -, to genome editing, where molecular alphabetical chiseling takes center stage. The use of CRISPR-Cas techniques is now flourishing, and bacterial immunity has given us humans a molecular toolbox where we can change a letter, seal or introduce a gap, tinker a correction, and many more precision tools that can deliver a healthier outcome over a morbid inheritance.

Newly studied offshoots of molecular systems for protection against bacteriophages come in the form of retrons, argonaut proteins, and many other effectors that can eliminate or curtail the prowess of the pathogen by targeted responses. Argonaute proteins require a "guard RNA" like sequence to zoom in on the threat at hand. For Argonaute proteins, the recognizing RNA molecules are somewhat shorter than in CRISPR-Cas systems, while not necessitating the presence of a Protospacer Adjacent Motif (PAM) next to the cutting sites for Cas protein binding [2].

Research on retrons is still at its infancy as the presence of retroelements in bacteria can be termed an unexpected discovery. Retrons are based on a reverse transcriptase (RT), a non-coding RNA (ncRNA) element and an effector protein and are speculated to be involved in anti-phage defenses - especially as second in line defensive units [3]. Toxin-antitoxins systems are also present in bacteria to nullify the dangers of toxins in the ambience.

5. Layered Defenses: Stepping up to the Call of Duty

The first line of defense – native/innate immunity - that relays into a second, more systemic and specific defensive mechanism is a trademark of most immune systems. In humans, the non-specific fortification of barriers, setting in motion armies of WBCs, and production of pathogen-perforating molecules form the first tier of immunity against the looming threat, prior to search and destruction based on unique molecular signatures. In plants, non-specific destruction is the prelude to SAR, forming the first layer of defense, while SAR provides the ramping up of the immune response holistically. In bacteria too, modification of cell wall components and signal responsive receptors can bolster bacterial immunity by fortifying the cell wall enclosed stronghold first and secondly by CRISPR-Cas systems that form a more comprehensive sequence-based cascade to destroy viral invaders, while perpetuating heritable immunity.

6. Physical Barriers: Building Citadels

Callose formation [Plants], modification of cell wall components [Bacteria], fibrin meshes trapping platelets [Humans] are examples of some of the physical barrier formations that epitomize the diverse responses that are provoked due to sensing of a pathogen in contact with an anatomical part. Here, the sensing is more primitive than precise and dependent on reciprocal contact and exposure.

7. Cell Death: A Worthwhile Sacrifice

Cell death is the preferred mode of action of the hypersensitivity reaction in plants where cells suspected to be infected with a virus are quickly destroyed along with the local tissue of concern, where both pathogen destruction as well as friendly fire can both be found. On this note, inflammation appears to hold the key in humans for WBCs to invade the locality of the infection and not let the infectious microorganism infiltrate into other parts of the anatomy. In immunity too, there is a mediatory process— like bacteria— where quorum sensing [the estimation of the relative density of immune cells in close contact and communication], and other mechanisms can trigger the regulation of immune responses by mediating gene expression using signal cascades and transcriptional factors.

8. Self versus non-self: Reading Barcodes

Pathogen-associated molecular patterns [PAMP] found in bacteria are ways unique conserved patterns are detected on invading organisms, using toll-like receptors that have convergent functionality in plants and humans [4]. PAMPs ensure that immunity is reactive, precise, calibrated to the correct levels, and will not cascade out of proportion, eliminating native tissues along the way. Antigen-antibody receptivity in human circulation is determined by the binding of antibodies to conformational [3-dimensional] and linear epitopes while the uniqueness of the response is mediated by the recombinational origin of antibodies [on the surface of B lymphocytes] as VDJ [variable Diversity Joining rearrangement] events, that lead to antibody diversity for the recognition of antigen determinants for concomitant binding, neutralization and macrophage recruitment.

9. Immunological Memory: A Mensa League

The faculty of immunological memory is shared by humans, plants, and bacteria. While in humans the antigen-dependent specification of immunity that is shared by many types of immunological cells [Macrophages, CD4+, CD8+ and Natural Killer

Cells etc] and proteins [Antibodies] form the backbone of how to deal with injurious intruders, that come in the form of viruses, stresses, prokaryotes, parasites and cancer cells. In bacteria, the Cas1-Cas2 enzyme system captures 30-40 nucleotide in length spacer regions for integration into a commonly accessed area of the bacterial genome, that forms a rapid cache for immunological retrieval to provide a quick response to an event of infection [5]. In plants, a programmed metamorphosis sets the stage for SAR that saddles immunological memory, where changes in signal generation, phytohormone-based metabolic and transcriptional events, epigenetic phenomena, as well as transgenerational events that are induced by immunological memory, and relayed to offspring as chemical modifications of nucleic acid molecules.

10. Induced Immunity: Empowering Antigens

While vaccines are now a mainstay in human infectious diseases, we should always remember that only Smallpox has been entirely eradicated from our planet and there are hundreds of other communicable morbidities [polio, guinea worm disease (Dracunculiasis), sleeping sickness, dengue and so forth], that require the intervention of application-oriented mechanisms that fit into Edison's Quadrant in terms of utility.

Plants can also be primed by the introduction of a benign effector molecule [such as siRNAs] that has a distinct and recognizable pattern for targeted destruction, while also empowering immunological memory against future attacks by the same pathogen. Post Transcriptional Gene Silencing [PTGS] in plants, the counterpart of RNAi in animals, works in the form of a siRNA-based suppression/inhibition to silence genes using sequence-specific binding to messenger RNA molecules.

Knowledge of bacterial immunity—how to best embolden CRISPR—Cas and other ancillary systems - will be beneficial to preserving prokaryotic cell lines kept in refrigerators where a single contamination from a bacteriophage can essentially harm decades-old work.

11. Epilogue: A Chessboard – Castles and Checkmates

Immunity begins as a virtual chess game and functions on the consensus that a threat is eliminated before the body becomes susceptible to being overwhelmed by disease. Ascendency from a simple "immunity" outlook to a more complex and precise course of action is the bread and butter of any immune response, and like bacteria and bacteriophages, there is a constant struggle for one to get the better of the other. Pathogenic viruses and parasites are constantly evolving methods to recruit/infect new hosts – either as species and as populations – and that means crossings of the zoonotic barrier such as in *Plasmodium knowlesi*, Ebola virus variants [Zaire, Sudan, Taï Forest, and Bundibugyo among others], the rising cases of Polio in refugee camps, the upheaval of Zika virus infections from a decade ago, and the reemergence of Chikungunya in Sri Lanka are all stories that capture scientific attention. However, the more viruses mutate, the more bacterial, human, and plant immune systems evolve to expand their protective tools.

For example, it may well be that natural killer cells begin as simple non-specific contenders to stop a pathogenic attack by using systems such as the Perforin/Granzyme Pathway, but with time developed a Mensa-like memory to remember the invasions with concomitant accuracy [6]. Evolution favors incremental steps and thrives on complexities, as nature is littered with stories that capture specificity – pollination syndromes of angiosperms, symbiotic relationships such as legumes and rhizobia, hypervariable regions in antibodies, CRISPR-Cas 9, olfactory reception in elephants, and evolution of teeth shapes and sizes. Immunity too would have begun non-specifically [around 1000 million years ago] [7] and honed on attributes during the next three periods - Ordovician, Silurian, and Devonian periods to improve the demarcation of self-versus non-self, deposit molecules – like spacers in caches – in genome regions that can be retrieved rapidly as memory, find ways for clonal expansion of benefactor cells, improve the robustness of the immune response, and to limit friendly fire in the form of collateral damage. Such adaptive measures are thought to have begun ~450 million years ago in jawed fishes, celebrating the advent of specificity in molecular toolboxes [8].

Immunity is a powerful weapon when used right. While the anti-vaccination drive battles the fundamentals of applied immunology, we as scientists should cultivate the trust the public has in science, to empower health and safety, over myth and fiction. The first COVID-19 vaccines under emergency authorization took 8 months for development and release; here, there was careful iteration of safety aspects despite the hastened pipeline. We are now technological messiahs, and the more we apply technology to basic biology, the more applied sciences such as vaccine biology will benefit from open-ended knowledge quests.

All animals have 28 essential elements of the periodic table, from 570 million years old *Dickensonia* to humans, like how Charles Darwin's magnum opus "Origin of Species By Natural Selection" has 26 letters of the alphabet in distinct arrangements. It was another Charles - Charles Dickens - who once quoted, *"I have never believed it possible that any natural or improved ability can claim immunity from the companionship of the steady, plain, hard-working qualities, and hope……".* Immunity is steady as well as quick to react, hard-working, and forms both the first line and last line of hope, and in that solemn truth is the discourse of biology with morbidity, and the lifeline granted by a high-spirited immunity, to outlast a slippery foe.

Immunity is a grandmaster in a lifelong chess game, and its Elo rating will always be valid during an infection as well as when primed by vaccination, when checkmate of the intruder is valued over acquiescence, protracting the distance of life, eliminating hurdles from a journey that needs restoration at several junctions.

Science will always be searching for the next Bobby Fischer, to transform basic science's potential into the next big frontier, transforming inbuilt immunity into yet another Swiss army knife, like how a *Streptococcus* immune system unveiled genome editing. Swiss army knives can have up to 141 blades/functions, while in the CasPDB database, 287 Cas proteins and 257,745 putative Cas proteins are available in 32,023 bacterial species and 1,802 archaeal contenders [9]. Add to that argonauts and retrons, then the field appears even bigger, broader, brighter, burlier and bolder, beefing up diversity, empowering choices

On a separate note, there are >25 lifesaving vaccines available according to the World Health Organization for key communicable diseases [https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases], while there are several in the pipeline, including newer ones for TB, Chikungunya, and Malaria among others. Smallpox in humans was eradicated in 1980, and Rinderpest in cattle in 2011, Guinea Worm disease is close to being eradicated, while Polio is known for its boomerang-like comebacks - the most recent in May 2025 in Papua New Guinea. I guess it is fair to say immunity will always have its share of David and Goliath moments, but they are few and far in-between. Unless we champion immunological breakthroughs and lend trust to science, we will not be gifted with reprieves from a cold, a recovery from a dengue infection, a recuperation from a tropical hemorrhagic fever, a rebounding from sickness to health, leaning on immunity's immutable vow, to shield and shelter.

Mensa international has 150,000 individuals while the immune system has ~1.8 trillion cells [10]; on the front of the collective IQ, the immune system wins but supplement to that ~10 nonillion viruses of which 270 viruses are known to infect humans, and the task seems herculean, nevertheless attainable. So, let's rally around immunity, trust its IQ for brainstorming, believe in its many tactical moves, honor every gambit, let reaction cascades triumph, and empower inbuilt treasures cancelling out invaders before they topple the bastion of life. So let these white knights shine in aegis, as stubborn preservationists. skillful warriors, and spirited combatants.

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