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POINT OF VIEW

Under the superficial dichotomy pathogen and allergen are two manifestations of same immune activation and pathogenesis mechanisms

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Abstract Pathogens and allergens are deemed as two contrasting facets of host immune status, deficiency and exuberant. *In silico* domain analysis of a diverse panel of pathogen and allergen proteins has revealed the shortcoming of this notion. Both the pathogen and allergen proteins elicit immune activation, with the outcome of immune agitation depending on the pathogen strain, allergen exposure duration, and host factors. Pathogens can replicate within the host and constantly irritate the immune system, leading to blood coagulation, respiratory collapse and death. Allergens, being non-viable, can only provoke the immune system transiently; however, depending on the allergen dose and extent exposed to, inflammation and fatality can occur. *In silico* analysis of pathogen and allergen proteins showed the conserved domains to be AAA, WR1, VKc, Kelch, Hr1, HAMP, HELICc, Dak2, CHAD, CHASE2, Galanin, PKS_TE, Robl_LC7, Excalibur, DISIN, etc. This exciting discovery can have far-reaching effects in drug target identification approaches.

Pathogens and allergens are conventionally considered as two ends of the pathogenesis continuum, while the former is associated with immunodeficiency, the latter is with autoimmunity.[1,2] This definition is only partially correct or even erroneous, in the wake of noble genomic discoveries.

Both the pathogenesis-inducing agents are tied to one mechanism of immune activation which leads to tissue or systemic inflammation.[3,4] The biggest difference between a pathogen and allergen lies in their in vivo replication ability, which the former is capable of and the latter is not.[5] Pathogen can invade the human body via different routes and proliferate, overwhelming the immune system. The outcome of the tussle between pathogen and immune system hinges on the strain vigour and host factors. Consequently

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the pathogen can undergo quiescence for a later favourable period; or get eliminated from the system; or manipulate the immune system to fatality.[6] Allergen on the other hand is a non-living macromolecule like proteins, lipids or polysaccharides from animal or plant origin (though metals, chemicals, drugs are allergens too, but not of organic source).[7,8] On exposure to it, allergen sensitises the immune system, and activates it, just like a pathogen does. As allergens are non-viable and not capable of self-propagation, the immune system is able to tackle it. However; a chronic encounter with the allergen agitates the immune system, leading to inflammation, endocrine perturbation, cancer, autoimmune diseases and neural pathologies.[9–11]

Unfortunately, very few experimental studies have drawn this parallel or shown the similarity between the pathogenesis-evoking mechanisms of pathogens and allergens. This author found the resemblance through *in silico* analysis of several virus (HIV, Hepatitis C, Ebola, dengue, zika), bacteria (*Escherichia coli*, *Mycobacterium tuberculosis*, *Pasteurella multocida*) and allergen (cockroach, pollen) proteins. The consensus protein domains in them were found to be AAA, WR1, VKc, Tryp_SPc, Kelch, Hr1, Knot1, HAMP, HELICc, DHDPS, Dak2, CHAD, CHASE2, BTAD, Galanin, GCK, PKS_TE, Robl_LC7, Excalibur, DISIN, Col_cuticle_N, DUF4208, etc. Most of these signature domains occur in enzymes, transcriptional factors and immune adhesion proteins. Occasional loss of the domains can be explained by genomic rearrangement due to stress faced, phylogenetic trajectories and resultant domain diversification. Further investigation in this aspect might set a new paradigm for drug discovery.

Conflict of interest statement

The author has no conflict of interest to declare.

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