



Tissue damage control underlies host tolerance to infection

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Immunity can be defined broadly as the inherent ability of any organism to protect itself from disease in general and from infectious diseases in particular. This evolutionarily conserved defense strategy relies on the recognition and cytotoxic targeting of pathogens, aiming at their containment and/or elimination. According to this notion, soluble molecules and cells involved in pathogen detection, containment and/or clearance are defined as the immune system. Over the years, it has become apparent however, that in some cases the immune system (as defined hereby) can become pathogenic, which is inconsistent with the definition of immunity itself, i.e. protection from disease. We reasoned that the pathologic outcome of infectious diseases reflects, in one way or another, the extent of tissue damage imposed by pathogens or by host molecules and cells involved in pathogen clearance. Depending on the extent of tissue damage, organ dysfunction might become apparent, as revealed by the clinical symptoms defining each infectious disease. Our data suggests that tissues have an intrinsic ability to limit the extent of damage imposed by pathogens or host factors involved in pathogen clearance. We refer to this protective mechanism as “tissue damage control” and posit that tissue damage control is an essential component of immunity that dissociates pathogen clearance from disease. Tissue damage control relies on stress-responsive programs that regulate the expression of genes conferring cellular metabolic adaptation, cytoprotection and/or tissue regeneration in response to specific forms of stress. We have demonstrated that expression of some of these stress-responsive genes is strictly required confer host tolerance to infection, that is, to provide tissue damage control and limit host disease severity irrespectively of pathogen load.

For more information go to: <http://www.igc.gulbenkian.pt/research/unit/43>