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Tissue Damage Control at the "Iron Age" of Host Microbe Interactions

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Damage control refers to actions made towards minimizing the extent of damage associated with a given emergency situation. Depending on context, damage control may refer to emergency procedures dealing with the sinking of a ship or to surgery procedures dealing with severe trauma or even to a company in Marvel Comics, which repairs damaged property arising from conflicts between super heroes and villains. By extension, "tissue" damage control refers to adaptive responses that minimize the extent of tissue damage and dysfunction associated with the pathogenesis of immune mediated inflammatory conditions, including in infectious diseases[1,2]. Presumably, tissue damage control is regulated by a number of evolutionarily conserved stress- and damage-responses associated with the induction of overlapping profiles of gene expression[1]. This argues for the existence of a core number of evolutionarily conserved genes regulating tissue damage control[1]. Moreover, this might explain why overlapping stress- and damage-responses confer protection against apparently unrelated forms of stress and damage, a phenomenon known as hormesis. A subgroup of these evolutionarily conserved genes regulates iron metabolism and control the participation of iron in the production of free radicals leading to oxidative stress and tissue dysfunction. In support of this notion, immune mediated inflammatory diseases are often associated with deregulated iron metabolism and oxidative stress[3,4]. Here I will discuss how the expression of stress responsive genes controlling iron metabolism exert anti-oxidant effects that confer tissue damage control in different infectious diseases[5-7].

References:

1. Soares, M.P. *et al.* (2014) Tissue damage control in disease tolerance. *Trends Immunol* 35 (10), 483-494
2. Medzhitov, R. *et al.* (2012) Disease tolerance as a defense strategy. *Science* 335 (6071), 936-941
3. Gozzelino, R. *et al.* (2010) Mechanisms of cell protection by heme oxygenase-1. *Annu Rev Pharmacol Toxicol* 50, 323-354

4. Soares, M.P. and Weiss, G. (2015) The Iron age of host-microbe interactions. *EMBO Rep* 16 (11), 1482-1500
5. Pamplona, A. *et al*. (2007) Heme oxygenase-1 and carbon monoxide suppress the pathogenesis of experimental cerebral malaria. *Nat Med* 13 (6), 703-710
6. Larsen, R. *et al*. (2010) A central role for free heme in the pathogenesis of severe sepsis. *Sci Transl Med* 2 (51), 51ra71
7. Ferreira, A. *et al*. (2011) Sickle Hemoglobin Confers Tolerance to Plasmodium Infection. *Cell* 145 (April 29), 398–409

BIOSKETCH

Dr. Miguel Che Parreira Soares

BS in biology (1990), MS in cellular biology (1994) and Ph.D. in Science (1995) from the University of Louvain in Belgium. Research fellow with Prof. Fritz H. Bach (1995-1998), Instructor in surgery (1998-2004) and Lecturer (2003-2004) at the Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA. Currently at Instituto Gulbekian de Ciência, Oeiras, Portugal (Since 2004) as a Principal Investigator. Invited professor at Lisbon Medical School, "Faculdade de Lisboa", Portugal (Since 2004). The research developed by of Miguel Soares laboratory aims at understanding the cellular and molecular mechanisms regulating inflammation and immunity and how these can be targeted therapeutically to overcome the pathologic outcome of immune mediated inflammatory diseases.

For more information:

Lab web page: http://www.igc.gulbenkian.pt/research/unit/43

CV: http://www.igc.gulbenkian.pt/groups/gi-m.soares/cv.pdf

Google scholar: http://scholar.google.com/citations?user=fZZu1ykAAAAJ

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Main original scientific contributions:

2014: That Specific components of the gut microbiota trigger a protective antibody response against malaria (*Cell 159 (6), 1277-1289*).

2012: That metabolic adaptation to tissue iron overload confers disease tolerance to systemic

infections (*Cell Host & Microbe 12; 5, 693-704*).

2011: That the sickle hemoglobin confers disease tolerance to malaria (*Cell, 2011, Vol. 145, Issue 3, 398-409, 29*).

2007-12: That specific stress-responses support the survival of an infected host irrespectively of its pathogen load, providing a molecular basis for disease tolerance to systemic infections such as malaria (*Nature Medicine, 2007, 13: 703-10 and Proc. Natl. Acad. Sci. USA. 2009, 106; 37: 15837-42*) and sepsis (*Science TM, 2010. 2: 51*; *Science, 2012, 335, 936*).

2007-10: That the gasotransmitter carbon monoxide (CO) prevents the pathogenic effects of heme (*Nature Medicine, 2007, 13:703-10 and Annu. Rev. Pharmacol. Toxicol. 2010. 50:323-54*).

2001-7: That the gasotransmitter carbon monoxide (CO) is protective against a broad range of

immune mediated inflammatory conditions, including the rejection of transplanted organs (*J. Immunol, 2001, 166, 4185-4194, Nature Medicine, 2003, 9, 183-190*), arteriosclerosis (*Nature Medicine, 2003, 9, 183-190*), ischemia & reperfusion injury (*The FASEB Journal. 2004; 18:771-772*), autoimmune neuroinflammation (*J. Clin. Invest. 2007, 117, 438-447*) and malaria (*Nature Medicine, 2007, 13: 703-10*).

1998-2001: That the gasotransmitter carbon monoxide (CO) is a cytoprotective (*J. Exp. Med., 2001, 192, 1015-25*) and regulates inflammation (*Nature Medicine, 2000, 6, 4, 422-428*).

1998: That transplanted organs can express "protective genes" prevent their own rejection (*Nature Medicine, 1998; 4, 91-8*).