

## Supplemental References

- S1. Bianchi, M.E., *HMGB1 loves company*. J Leukoc Biol, 2009. **86**(3): p. 573-6.
- S2. Kazama, H., et al., *Induction of immunological tolerance by apoptotic cells requires caspase-dependent oxidation of high-mobility group box-1 protein*. Immunity, 2008. **29**(1): p. 21-32.
- S3. Yang, H., et al., *Redox modification of cysteine residues regulates the cytokine activity of HMGB1*. Mol Med, 2011.
- S4. Yang, H., et al., *A critical cysteine is required for HMGB1 binding to Toll-like receptor 4 and activation of macrophage cytokine release*. Proc Natl Acad Sci U S A, 2010. **107**(26): p. 11942-7.
- S5. Andersson, U. and K.J. Tracey, *HMGB1 is a therapeutic target for sterile inflammation and infection*. Annu Rev Immunol, 2011. **29**: p. 139-62.
- S6. Yang, H. and K.J. Tracey, *Targeting HMGB1 in inflammation*. Biochim Biophys Acta, 2010. **1799**(1-2): p. 149-56.
- S7. Levy, R.M., et al., *Systemic inflammation and remote organ injury following trauma require HMGB1*. Am J Physiol Regul Integr Comp Physiol, 2007. **293**(4): p. R1538-44.
- S8. Yang, R., et al., *Anti-HMGB1 neutralizing antibody ameliorates gut barrier dysfunction and improves survival after hemorrhagic shock*. Mol Med, 2006. **12**(4-6): p. 105-14.
- S9. Kim, J.Y., et al., *HMGB1 contributes to the development of acute lung injury after hemorrhage*. Am J Physiol Lung Cell Mol Physiol, 2005. **288**(5): p. L958-65.
- S10. Gibot, S., et al., *High-mobility group box 1 protein plasma concentrations during septic shock*. Intensive Care Med, 2007. **33**(8): p. 1347-53.
- S11. Yang, H., et al., *Reversing established sepsis with antagonists of endogenous high-mobility group box 1*. Proc Natl Acad Sci U S A, 2004. **101**(1): p. 296-301.
- S12. Wang, H., et al., *HMGB1 as a late mediator of lethal systemic inflammation*. Am J Respir Crit Care Med, 2001. **164**(10 Pt 1): p. 1768-73.
- S13. Wang, H., et al., *HMG-1 as a late mediator of endotoxin lethality in mice*. Science, 1999. **285**(5425): p. 248-51.
- S14. Muhammad, S., et al., *The HMGB1 receptor RAGE mediates ischemic brain damage*. J Neurosci, 2008. **28**(46): p. 12023-31.
- S15. Liu, K., et al., *Anti-high mobility group box 1 monoclonal antibody ameliorates brain infarction induced by transient ischemia in rats*. FASEB J, 2007. **21**(14): p. 3904-16.
- S16. Goldstein, R.S., et al., *Elevated high-mobility group box 1 levels in patients with cerebral and myocardial ischemia*. Shock, 2006. **25**(6): p. 571-4.

- S17. Andrassy, M., et al., *High-mobility group box-1 in ischemia-reperfusion injury of the heart*. Circulation, 2008. **117**(25): p. 3216-26.
- S18. Ilmakunnas, M., et al., *High mobility group box 1 protein as a marker of hepatocellular injury in human liver transplantation*. Liver Transpl, 2008. **14**(10): p. 1517-25.
- S19. Tsung, A., et al., *HMGB1 release induced by liver ischemia involves Toll-like receptor 4 dependent reactive oxygen species production and calcium-mediated signaling*. J Exp Med, 2007. **204**(12): p. 2913-23.
- S20. Tsung, A., et al., *The nuclear factor HMGB1 mediates hepatic injury after murine liver ischemia-reperfusion*. J Exp Med, 2005. **201**(7): p. 1135-43.
- S21. Schierbeck, H., et al., *Monoclonal anti-HMGB1 antibody protection in two experimental arthritis models*. Mol Med, 2011.
- S22. Ostberg, T., et al., *Protective targeting of high mobility group box chromosomal protein 1 in a spontaneous arthritis model*. Arthritis Rheum, 2010. **62**(10): p. 2963-72.
- S23. Pisetsky, D.S., H. Erlandsson-Harris, and U. Andersson, *High-mobility group box protein 1 (HMGB1): an alarmin mediating the pathogenesis of rheumatic disease*. Arthritis Res Ther, 2008. **10**(3): p. 209.
- S24. Urbonaviciute, V., et al., *Induction of inflammatory and immune responses by HMGB1-nucleosome complexes: implications for the pathogenesis of SLE*. J Exp Med, 2008. **205**(13): p. 3007-18.
- S25. Andersson, A., et al., *Pivotal advance: HMGB1 expression in active lesions of human and experimental multiple sclerosis*. J Leukoc Biol, 2008. **84**(5): p. 1248-55.
- S26. Zhang, S., et al., *HMGB1, an innate alarmin, in the pathogenesis of type 1 diabetes*. Int J Clin Exp Pathol, 2009. **3**(1): p. 24-38.
- S27. Maroso, M., et al., *Toll-like receptor 4 and high-mobility group box-1 are involved in ictogenesis and can be targeted to reduce seizures*. Nat Med, 2010. **16**(4): p. 413-9.
- S28. Taguchi, A., et al., *Blockade of RAGE-amphoterin signalling suppresses tumour growth and metastases*. Nature, 2000. **405**(6784): p. 354-60.
- S29. Curtin, J.F., et al., *HMGB1 mediates endogenous TLR2 activation and brain tumor regression*. PLoS Med, 2009. **6**(1): p. e10.
- S30. Apetoh, L., et al., *Toll-like receptor 4-dependent contribution of the immune system to anticancer chemotherapy and radiotherapy*. Nat Med, 2007. **13**(9): p. 1050-9.
- S31. Limana, F., et al., *HMGB1 attenuates cardiac remodelling in the failing heart via enhanced cardiac regeneration and miR-206-mediated inhibition of TIMP-3*. PLoS One, 2011. **6**(6): p. e19845.
- S32. Kohno, T., et al., *Role of high-mobility group box 1 protein in post-infarction healing process and left ventricular remodelling*. Cardiovasc Res, 2009. **81**(3): p. 565-73.

- S33. Germani, A., F. Limana, and M.C. Capogrossi, *Pivotal advances: high-mobility group box 1 protein--a cytokine with a role in cardiac repair*. J Leukoc Biol, 2007. **81**(1): p. 41-5.
- S34. Limana, F., et al., *Exogenous high-mobility group box 1 protein induces myocardial regeneration after infarction via enhanced cardiac C-kit+ cell proliferation and differentiation*. Circ Res, 2005. **97**(8): p. e73-83.
- S35. Biscetti, F., et al., *High-mobility group box-1 protein promotes angiogenesis after peripheral ischemia in diabetic mice through a VEGF-dependent mechanism*. Diabetes, 2010. **59**(6): p. 1496-505.
- S36. Straino, S., et al., *High-mobility group box 1 protein in human and murine skin: involvement in wound healing*. J Invest Dermatol, 2008. **128**(6): p. 1545-53.
- S37. Yang, J., et al., *HMGB1 is a bone-active cytokine*. J Cell Physiol, 2008. **214**(3): p. 730-9.
- S38. Taniguchi, N., et al., *Stage-specific secretion of HMGB1 in cartilage regulates endochondral ossification*. Mol Cell Biol, 2007. **27**(16): p. 5650-63.
- S39. De Mori, R., et al., *Multiple effects of high mobility group box protein 1 in skeletal muscle regeneration*. Arterioscler Thromb Vasc Biol, 2007. **27**(11): p. 2377-83.
- S40. Huttunen, H.J., et al., *Coregulation of neurite outgrowth and cell survival by amphoterin and S100 proteins through receptor for advanced glycation end products (RAGE) activation*. J Biol Chem, 2000. **275**(51): p. 40096-105.
- S41. van Zoelen, M.A., et al., *Expression and role of myeloid-related protein-14 in clinical and experimental sepsis*. Am J Respir Crit Care Med, 2009. **180**(11): p. 1098-106.
- S42. Vogl, T., et al., *Mrp8 and Mrp14 are endogenous activators of Toll-like receptor 4, promoting lethal, endotoxin-induced shock*. Nat Med, 2007. **13**(9): p. 1042-9.
- S43. Wittkowski, H., et al., *Neutrophil-derived S100A12 in acute lung injury and respiratory distress syndrome*. Crit Care Med, 2007. **35**(5): p. 1369-75.
- S44. Kikkawa, T., et al., *Significance of measuring S100A12 and sRAGE in the serum of sepsis patients with postoperative acute lung injury*. Dig Surg, 2010. **27**(4): p. 307-12.
- S45. Yang, Z., et al., *S100A12 provokes mast cell activation: a potential amplification pathway in asthma and innate immunity*. J Allergy Clin Immunol, 2007. **119**(1): p. 106-14.
- S46. Grevers, L.C., et al., *S100A8 enhances osteoclastic bone resorption in vitro through activation of Toll-like receptor 4: implications for bone destruction in murine antigen-induced arthritis*. Arthritis Rheum, 2011. **63**(5): p. 1365-75.
- S47. Zreiqat, H., et al., *S100A8 and S100A9 in experimental osteoarthritis*. Arthritis Res Ther, 2010. **12**(1): p. R16.

- S48. van Lent, P.L., et al., *S100A8 causes a shift toward expression of activatory Fc<sub>gamma</sub> receptors on macrophages via toll-like receptor 4 and regulates Fc<sub>gamma</sub> receptor expression in synovium during chronic experimental arthritis*. Arthritis Rheum, 2010. **62**(11): p. 3353-64.
- S49. Hammer, H.B., et al., *Calprotectin (a major S100 leucocyte protein) predicts 10-year radiographic progression in patients with rheumatoid arthritis*. Ann Rheum Dis, 2010. **69**(1): p. 150-4.
- S50. Foell, D., H. Wittkowski, and J. Roth, *Mechanisms of disease: a 'DAMP' view of inflammatory arthritis*. Nat Clin Pract Rheumatol, 2007. **3**(7): p. 382-90.
- S51. Foell, D. and J. Roth, *Proinflammatory S100 proteins in arthritis and autoimmune disease*. Arthritis Rheum, 2004. **50**(12): p. 3762-71.
- S52. Youssef, P., et al., *Expression of myeloid related proteins (MRP) 8 and 14 and the MRP8/14 heterodimer in rheumatoid arthritis synovial membrane*. J Rheumatol, 1999. **26**(12): p. 2523-8.
- S53. Rouleau, P., et al., *The calcium-binding protein S100A12 induces neutrophil adhesion, migration, and release from bone marrow in mouse at concentrations similar to those found in human inflammatory arthritis*. Clin Immunol, 2003. **107**(1): p. 46-54.
- S54. Wittkowski, H., et al., *S100A12 is a novel molecular marker differentiating systemic-onset juvenile idiopathic arthritis from other causes of fever of unknown origin*. Arthritis Rheum, 2008. **58**(12): p. 3924-31.
- S55. Ryckman, C., et al., *Role of S100A8 and S100A9 in neutrophil recruitment in response to monosodium urate monohydrate crystals in the air-pouch model of acute gouty arthritis*. Arthritis Rheum, 2003. **48**(8): p. 2310-20.
- S56. Croce, K., et al., *Myeloid-related protein-8/14 is critical for the biological response to vascular injury*. Circulation, 2009. **120**(5): p. 427-36.
- S57. Foell, D., et al., *Early recruitment of phagocytes contributes to the vascular inflammation of giant cell arteritis*. J Pathol, 2004. **204**(3): p. 311-6.
- S58. Hofmann Bowman, M.A., et al., *S100A12 in vascular smooth muscle accelerates vascular calcification in apolipoprotein E-null mice by activating an osteogenic gene regulatory program*. Arterioscler Thromb Vasc Biol, 2011. **31**(2): p. 337-44.
- S59. Lorenz, E., et al., *Different expression ratio of S100A8/A9 and S100A12 in acute and chronic lung diseases*. Respir Med, 2008. **102**(4): p. 567-73.
- S60. Seeliger, S., et al., *Expression of calcium-binding proteins MRP8 and MRP14 in inflammatory muscle diseases*. Am J Pathol, 2003. **163**(3): p. 947-56.
- S61. Goova, M.T., et al., *Blockade of receptor for advanced glycation end-products restores effective wound healing in diabetic mice*. Am J Pathol, 2001. **159**(2): p. 513-25.

- S62. Eming, S.A., et al., *Differential proteomic analysis distinguishes tissue repair biomarker signatures in wound exudates obtained from normal healing and chronic wounds*. J Proteome Res, 2010. **9**(9): p. 4758-66.
- S63. Gebhardt, C., et al., *S100A8 and S100A9 in inflammation and cancer*. Biochem Pharmacol, 2006. **72**(11): p. 1622-31.
- S64. Coffelt, S.B. and A.B. Scandurro, *Tumors sound the alarmin(s)*. Cancer Res, 2008. **68**(16): p. 6482-5.
- S65. Hiratsuka, S., et al., *The S100A8-serum amyloid A3-TLR4 paracrine cascade establishes a pre-metastatic phase*. Nat Cell Biol, 2008. **10**(11): p. 1349-55.
- S66. Salama, I., et al., *A review of the S100 proteins in cancer*. Eur J Surg Oncol, 2008. **34**(4): p. 357-64.
- S67. Caldwell, R.L., et al., *Tissue profiling MALDI mass spectrometry reveals prominent calcium-binding proteins in the proteome of regenerative MRL mouse wounds*. Wound Repair Regen, 2008. **16**(3): p. 442-9.
- S68. Trostrup, H., et al., *S100A8/A9 deficiency in nonhealing venous leg ulcers uncovered by multiplexed antibody microarray profiling*. Br J Dermatol, 2011. **165**(2): p. 292-301.
- S69. Wu, N. and J.M. Davidson, *Migration inhibitory factor-related protein (MRP)8 and MRP14 are differentially expressed in free-electron laser and scalpel incisions*. Wound Repair Regen, 2004. **12**(3): p. 327-36.
- S70. Chiba, M., et al., *Elevation and characteristics of Rab30 and S100a8/S100a9 expression in an early phase of liver regeneration in the mouse*. Int J Mol Med, 2011. **27**(4): p. 567-74.
- S71. Donato, R., et al., *S100B's double life: intracellular regulator and extracellular signal*. Biochim Biophys Acta, 2009. **1793**(6): p. 1008-22.
- S72. Hu, J., et al., *S100 beta stimulates inducible nitric oxide synthase activity and mRNA levels in rat cortical astrocytes*. J Biol Chem, 1996. **271**(5): p. 2543-7.
- S73. Kochanek, P.M., et al., *Biomarkers of primary and evolving damage in traumatic and ischemic brain injury: diagnosis, prognosis, probing mechanisms, and therapeutic decision making*. Curr Opin Crit Care, 2008. **14**(2): p. 135-41.
- S74. Beer, C., et al., *Systemic markers of inflammation are independently associated with S100B concentration: results of an observational study in subjects with acute ischaemic stroke*. J Neuroinflammation, 2010. **7**: p. 71.
- S75. Gruden, M.A., et al., *Differential neuroimmune markers to the onset of Alzheimer's disease neurodegeneration and dementia: autoantibodies to Abeta(25-35) oligomers, S100b and neurotransmitters*. J Neuroimmunol, 2007. **186**(1-2): p. 181-92.
- S76. Schroeter, M.L., et al., *Neuron-specific enolase is unaltered whereas S100B is elevated in serum of patients with schizophrenia--original research and meta-analysis*. Psychiatry Res, 2009. **167**(1-2): p. 66-72.
- S77. Iwasaki, Y., T. Shiojima, and M. Kinoshita, *S100 beta prevents the death of motor neurons in newborn rats after sciatic nerve section*. J Neurol Sci, 1997. **151**(1): p. 7-12.

- S78. Bangen, J.M., F.U. Schade, and S.B. Flohe, *Diverse regulatory activity of human heat shock proteins 60 and 70 on endotoxin-induced inflammation*. Biochem Biophys Res Commun, 2007. **359**(3): p. 709-15.
- S79. Broere, F., R. van der Zee, and W. van Eden, *Heat shock proteins are no DAMPs, rather 'DAMPERS'*. Nat Rev Immunol, 2011. **11**(8): p. 565; author reply 565.
- S80. Yang, D., et al., *Multiple roles of antimicrobial defensins, cathelicidins, and eosinophil-derived neurotoxin in host defense*. Annu Rev Immunol, 2004. **22**: p. 181-215.
- S81. Doss, M., et al., *Human defensins and LL-37 in mucosal immunity*. J Leukoc Biol, 2010. **87**(1): p. 79-92.
- S82. Heilborn, J.D., et al., *The cathelicidin anti-microbial peptide LL-37 is involved in re-epithelialization of human skin wounds and is lacking in chronic ulcer epithelium*. J Invest Dermatol, 2003. **120**(3): p. 379-89.
- S83. Claus, R.A., et al., *Approaching clinical reality: markers for monitoring systemic inflammation and sepsis*. Curr Mol Med, 2010. **10**(2): p. 227-35.
- S84. Wittkowski, H., et al., *Effects of intra-articular corticosteroids and anti-TNF therapy on neutrophil activation in rheumatoid arthritis*. Ann Rheum Dis, 2007. **66**(8): p. 1020-5.
- S85. Hammer, H.B., et al., *Calprotectin (a major leucocyte protein) is strongly and independently correlated with joint inflammation and damage in rheumatoid arthritis*. Ann Rheum Dis, 2007. **66**(8): p. 1093-7.
- S86. Prakken, B., S. Albani, and A. Martini, *Juvenile idiopathic arthritis*. Lancet, 2011. **377**(9783): p. 2138-49.
- S87. Kane, D., et al., *Increased perivascular synovial membrane expression of myeloid-related proteins in psoriatic arthritis*. Arthritis Rheum, 2003. **48**(6): p. 1676-85.
- S88. Brun, J.G., et al., *Sjogren's syndrome in inflammatory rheumatic diseases: analysis of the leukocyte protein calprotectin in plasma and saliva*. Scand J Rheumatol, 1994. **23**(3): p. 114-8.
- S89. Wittkowski, H., et al., *MRP8 and MRP14, phagocyte-specific danger signals, are sensitive biomarkers of disease activity in cryopyrin-associated periodic syndromes*. Ann Rheum Dis, 2011.
- S90. Kallinich, T., et al., *Neutrophil-derived S100A12 as novel biomarker of inflammation in familial Mediterranean fever*. Ann Rheum Dis, 2010. **69**(4): p. 677-82.
- S91. Vince, R.V., et al., *Hypoxia mediated release of endothelial microparticles and increased association of S100A12 with circulating neutrophils*. Oxid Med Cell Longev, 2009. **2**(1): p. 2-6.
- S92. Foell, D., et al., *S100A12 (EN-RAGE) in monitoring Kawasaki disease*. Lancet, 2003. **361**(9365): p. 1270-2.
- S93. Foell, D., H. Wittkowski, and J. Roth, *Monitoring disease activity by stool analyses: from occult blood to molecular markers of intestinal inflammation and damage*. Gut, 2009. **58**(6): p. 859-68.

- S94. Rosenberg, H.F., *HMGB1, a novel biomarker of inflammatory demyelinating disease: an interview with Dr. Robert A. Harris.* J Leukoc Biol, 2008. **84**(5): p. 1256-8.
- S95. Barnay-Verdier, S., et al., *Emergence of autoantibodies to HMGB1 is associated with survival in patients with septic shock.* Intensive Care Med, 2011. **37**(6): p. 957-62.
- S96. Huang, L.F., et al., *Association of high mobility group box-1 protein levels with sepsis and outcome of severely burned patients.* Cytokine, 2011. **53**(1): p. 29-34.
- S97. Cohen, M.J., et al., *Early release of high mobility group box nuclear protein 1 after severe trauma in humans: role of injury severity and tissue hypoperfusion.* Crit Care, 2009. **13**(6): p. R174.
- S98. Peltz, E.D., et al., *HMGB1 is markedly elevated within 6 hours of mechanical trauma in humans.* Shock, 2009. **32**(1): p. 17-22.
- S99. Peter, K. and A. Bobik, *HMGB1 signals danger in acute coronary syndrome: Emergence of a new risk marker for cardiovascular death?* Atherosclerosis, 2011.