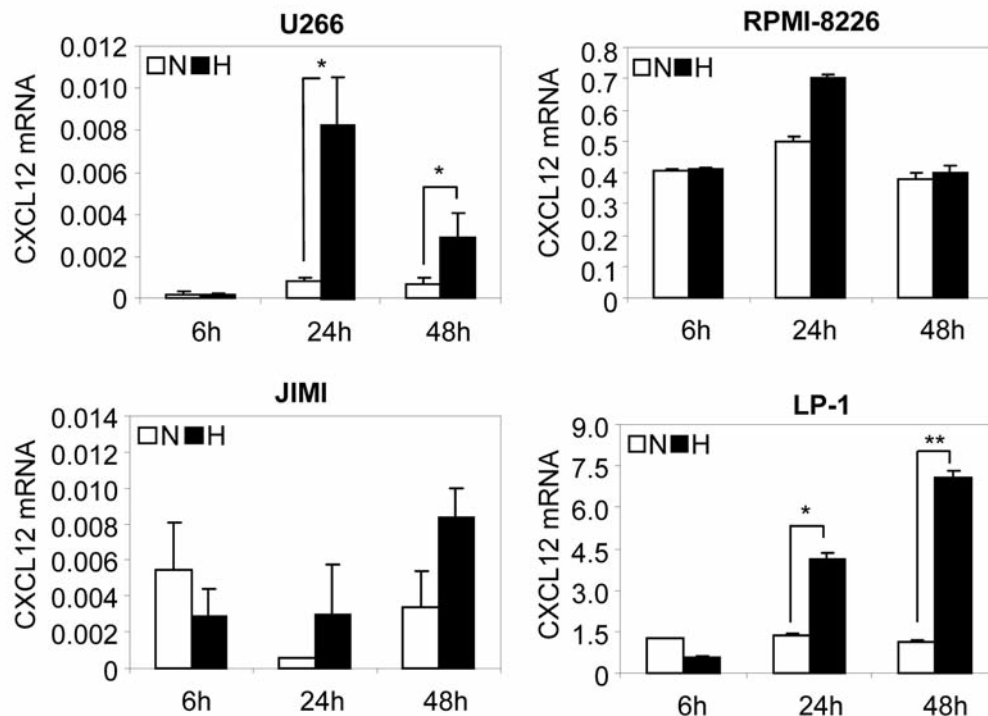


Hypoxia-inducible factor-2 is a novel regulator of aberrant CXCL12 expression in multiple myeloma plasma cells

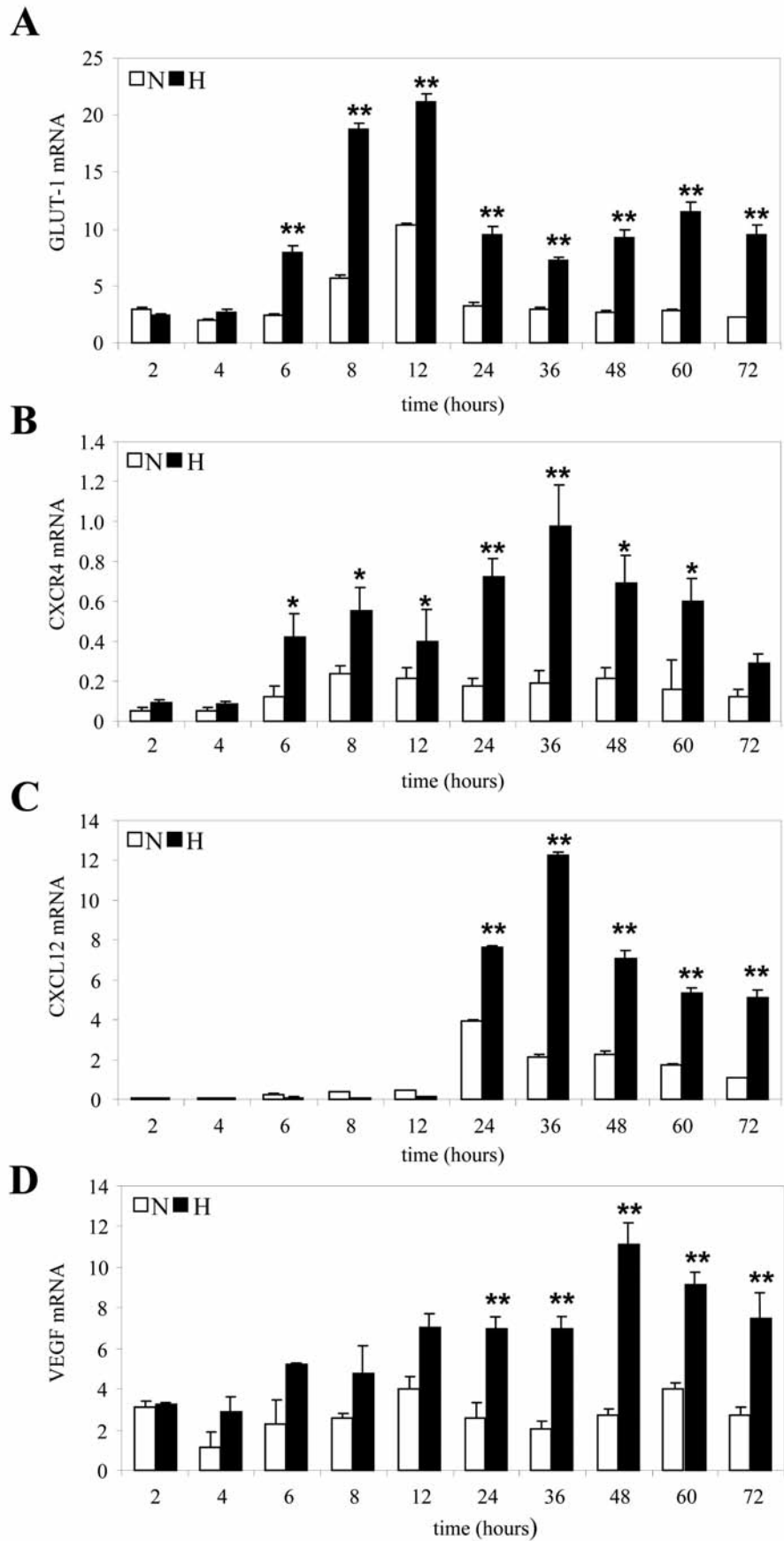
Sally K. Martin,¹ Peter Diamond,¹ Sharon A. Williams,¹ Luen Bik To,¹ Daniel J. Peet,² Nobutaka Fujii,³ Stan Gronthos,⁴ Adrian L. Harris,⁵ and Andrew C.W. Zannettino¹

¹Myeloma Research Program, Division of Haematology, Centre for Cancer Biology–SA Pathology and University of Adelaide, Australia; ²Department of Molecular Bioscience, University of Adelaide, Australia; ³Department of Bioorganic Medicinal Chemistry, Graduate School of Pharmaceutical Sciences, Kyoto University, Japan; ⁴Mesenchymal Stem Cell Group, Division of Haematology, Hanson Institute, CSCR and University of Adelaide, Australia, and ⁵Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, UK

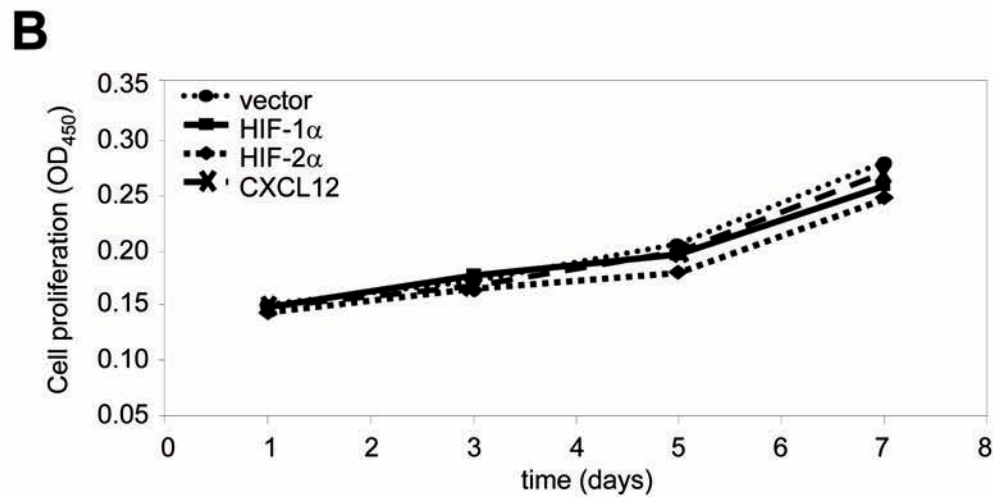
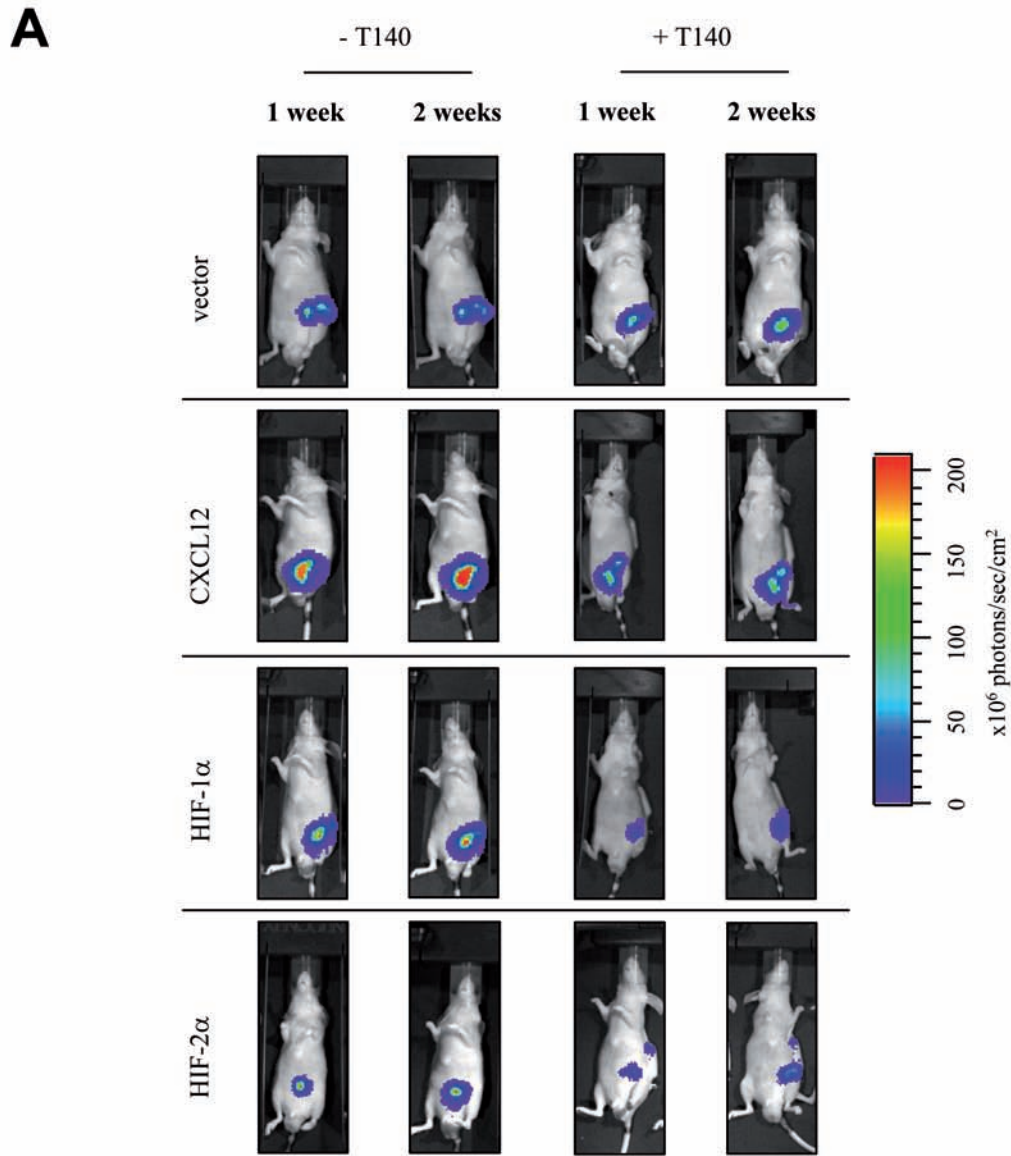
Citation: Martin SK, Diamond P, Williams SA, To LB, Peet DJ, Fujii N, Gronthos S, Harris AL, and Zannettino ACW. Hypoxia-inducible factor-2 is a novel regulator of aberrant CXCL12 expression in multiple myeloma plasma cells. *Haematologica* 2010; 95:776-784. doi:10.3324/haematol.2009.015628



Online Supplementary Figure S1. Hypoxic regulation of CXCL12 expression in human MM cell lines. Levels of CXCL12 mRNA expression were measured in U266, RPMI-8226, JIMI and LP-1 MM plasma cell lines following 6, 24 and 48 h of normoxic (white bars) or hypoxic (black bars) culture. Columns, mean (n=3); bars, SEM. *P<0.05, **P<0.005.



Online Supplementary Figure S2. Hypoxic regulation of *CXCL12*, *GLUT-1*, *CXCR4* and *VEGF* expression in LP-1 cells. *CXCL12*, *GLUT1*, *CXCR4* and *VEGF* mRNA expression was measured in LP-1 cells cultured under normoxic (white bars) or hypoxic (black bars) conditions for up to 72 h. Columns, mean (n=3); bars, SEM. * $P < 0.05$, ** $P < 0.005$.



Online Supplementary Figure S3. The *in vivo* and *in vitro* growth of CXCL12-, HIF-1 α - and HIF-2 α - over-expressing LP-1 cells. (A) CXCL12-, HIF-1 α - or HIF-2 α -over-expressing LP-1 cells were injected subcutaneously in a Matrigel plug into mice (n=12/group), and half of the mice were administered the CXCR4 antagonist, T140. Tumor growth was monitored weekly for 2 weeks using bioluminescence imaging. (B) The rate of *in vitro* proliferation of CXCL12-, HIF-1 α - or HIF-2 α - over-expressing LP-1 cells was assessed using WST-1. Lines, mean (n=4). P>0.05 (NS).