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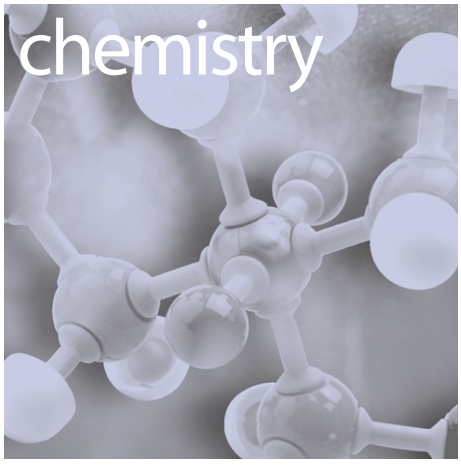
monitor



MOLECULES

Novel antitumour small molecule Inhibitors of hypoxia-inducible factor-1

Developing solid tumours are characterized by areas of hypoxia (low oxygen tension) that are commonly associated with an aggressive and metastatic cancer phenotype frequently linked to a poor response to radio- or chemo-therapy. Areas of low oxygen tension act as a stimulus for genes involved in proliferation, glycolysis and angiogenesis. A particularly important transcription factor involved in the regulation of hypoxia-activated genes is hypoxia-inducible factor-1 (HIF-1); and the HIF-1 subunit HIF-1α has emerged in recent years as an important anticancer drug target [1, 2].

Chau and co-workers (Institute of Cancer Research, Sutton, UK) have reported the development of U2OS human osteosarcoma cells that stably express a luciferase reporter construct under the control of a hypoxia response element (U2OS-HRE-luc) [3]. The group have used this construct in a high-throughput cellular screening assay to identify HIF-1 inhibitory compounds following HIF-1 induction with a hypoxia mimetic (deferoxamine mesylate). A pilot screen of the National Cancer Institute Diversity Set of 2,000 compounds led to the identification of two novel hit compounds, **(i)** and **(ii)**, which had not previously been found in previous hypoxia screens. Interestingly, the two molecules differentially blocked HIF-1 activity and HIF-1α induction in response to hypoxic stress and insulin-like growth factor-1.

1 Semenza, G.L. (2003) Targeting HIF-1 for cancer therapy. *Nat. Rev. Cancer* 3, 721–732
2 Hewitson, K.S and Schofield, C.J. (2004) The HIF pathway as a therapeutic target. *Drug Disc. Today* 9, 704-711
3 Chau, N-M. *et al.* (2005) Identification of novel small molecule inhibitors of hypoxia-inducible factor-1 that differentially block hypoxia-inducible factor-1 activity and hypoxia-inducible factor-1α induction in response to hypoxic stress and growth factors. *Cancer Res.* 65, 4918–4928

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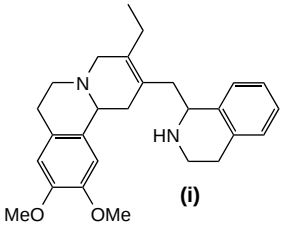
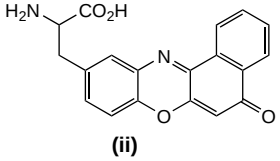


(i)



(ii)

MICROBIOLOGY

Universal vaccine and novel surface structure identified by Group B *Streptococcus* genomics

Group B *Streptococcus* (GBS) is a multiserotype bacterium that colonizes the anogenital mucosa of healthy women. GBS is the major cause of serious infections in newborns despite antibiotic prophylaxis. Because maternal antibodies against GBS reduce the risk of neonatal infection, vaccination of the mother has the potential to reduce the incidence of infection.

Maione *et al.* [2] mined for potential vaccine candidates by comparing the whole genomes of eight GBS strains of five different serotypes. A 'core' of ≈80% of the genes were conserved between strains whereas the remainder was variable. 312 proteins predicted to be extracellular were successfully expressed in *Escherichia coli* and used to immunize female mice. Mice were mated and the offspring was challenged with GBS. This screening identified one protein from the core genome (GBS322) and three from the variable (GBS67, GBS80, and GBS104) that significantly increased the survival of the mice. Immunization with each antigen gave protection against more than

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