Crystal Structures of Autocrine Motility Factor Complexed with Inhibitors

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Autocrine motility factor (AMF), a tumor-secreted cytokine, stimulates cell migration *in vitro* and metastasis *in vivo*. AMF is identical to the extracellular cytokines neuroleukin and maturation factor and, interestingly, to the intracellular enzyme phosphoglucose isomerase. Cytokine activity of AMF is inhibited by carbohydrate compounds, as they compete for AMF binding with the carbohydrate moiety of the AMF receptor, which is a glycosylated seven-transmembrane helix protein. Crystal structure analyses and site-directed mutagenesis studies of human AMF revealed that the regions important for the enzymatic function of AMF/PGI overlap those for the cytokine function of AMF [1].

Here we have determined the crystal structures of the various length of inhibitor-bound AMF at high resolution and assayed the inhibitory activities of the various inhibitors. These data provide an insight into the lead compound design of more effective AMF inhibitors.

[1] Tanaka N., Haga A., Uemura H., Akiyama H., Funasaka T., Nagase H., Raz A., Nakamura K.T., *J. Mol. Biol.*, 2002, **318**, 985.

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