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High yield production of CD74 constructs fused to solubility-enhancing peptides and characterization of their MIF-binding capacities

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The IF receptor, CD74, has been shown to be involved in many biological processes amongst which antigen loading and transport of MHC class II molecules from endoplasmic reticulum to Golgi complex. It is also part of a receptor complex binding to macrophage migration inhibitory factor (MIF), and participates in inflammatory signaling. Inhibition of MIF-CD74 complex formation is regarded as a potentially attractive therapeutic target in inflammation and cancer. In order to be able to produce large quantities of the extracellular moiety of human CD74, which has been reported to be unstable and protease-sensitive, different constructs were made as fusions with two solubility enhancers: the well-known maltose-binding domain and Fh8, a small protein secreted by parasite *Fasciola hepatica*. The fusion proteins could be purified with high yields from *Escherichia coli* and were demonstrated to be active in binding to MIF. In order to identify MIF binding compound that potentially interfere with MIF-CD74 interaction, we performed a substitution-oriented screening on a library of chromene compounds (inspired by Orita-13). MIF tautomerase inhibitors with IC₅₀'s in low micromolar range were identified. These novel inhibitors of the MIF tautomerase activity may ultimately support the development of novel therapeutic agents against diseases in which MIF is involved.

Biography

Tjje Kok is doing his PhD at University of Groningen, The Netherlands (2014-2018). He is previously the vice dean of Faculty of Biotechnology, University of Surabaya, Indonesia (2011-2014). In 2005-2010, he was a member of American Chemical Society (ACS). He has published more than 15 papers in national journals in Indonesia and 2 papers in reputed journals (*Protein Expression and Purification journal*, and *Bioorganic and Medicinal Chemistry journal*); in addition, one paper is now under review in *Drug Discovery Today* journal. At present, he is serving as a reviewer of African Journal of Pharmacy and Pharmacology.

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