



Identification of novel compounds that inhibit S100P and RAGE binding as a new therapy for Pancreatic Cancer

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Pancreatic adenocarcinoma (PDAC) is one of the most lethal human cancers with a 5-year survival of less than 5% due mostly to the lack of effective therapy and difficulty of detection at an early stage of development. Recent studies have shown a high prevalence of S100 proteins in PDAC, in particular the calcium-binding protein S100P. It has been proposed that the metastasis-promoting calcium-binding protein S100P, which possesses both intracellular and extracellular functions, activates key cell signaling pathways, including MAP kinase and nuclear factor NF κ B pathways through its extracellular interaction with the receptor for advanced glycation end products (RAGE). The interaction between RAGE-S100P stimulates pancreatic tumor proliferation, survival, invasion and metastasis progression in vitro and tumor metastasis in vivo. Using computational chemistry methods, our laboratory have identified 87 novel compounds that prevent S100P binding to RAGE. Here in this talk we will outline the key challenges and methodology used to validate an ELISA to measure S100P and RAGE interaction. Our initial results highlight 22 new lead compounds that inhibit S100P-RAGE interaction, some of which have shown an ability to decrease pancreatic cell line growth. This work is supported by Worldwide Cancer Research and the University of Hertfordshire.

Biography

Dr Louise Mackenzie completed her PhD at the age of 29 at Imperial College, London, and continued in postdoctoral study at Imperial College and the William Harvey Research Institute. Currently a Senior lecturer in Pharmacology at the University of Hertfordshire, Louise has published 22 Full Papers and 5 Review Articles in reputed journals.