

## **S100A8/A9 and its novel receptors play a critical part in organ tropic cancer metastasis**

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Cancer cells frequently show organ specific metastasis, in which the "seed and soil" theory has long been proposed. In this concept, it has first reported that S100A8/A9, a heterodimer complex composed of S100A8 and S100A9 proteins, which exhibits a "soil signal", produced and secreted from the lung in the tumor-bearing body works as a strong ligand to a soil sensor, TLR4, presented on cancer cells, in which the S100A8/A9-TLR4 binding leads cancer cells to metastasize the lung area where S100A8/A9 is abundant. In addition, RAGE was also included as a soil sensor for the S100A8/A9-mediated lung tropic cancer metastasis. Besides to these receptors, we recently showed the presence of novel soil sensors for S100A8/A9, namely; EMMPRIN, NPTN, ALCAM and MCAM. We then referred to these collections of receptor proteins as "novel S100 Soil Sensor Receptors (novel SSSRs)". In this presentation we hence introduce a crucial role of S100A8/A9-novel SSSRs axis on cancer metastasis. The bindings of S100A8/A9 to individual SSSRs play an important part in cancer metastasis through upregulation of cellular motility and invasiveness of cancer cells. To take the metastatic force away from cancer cells, we developed novel biologics that prevent interaction of S100A8/A9 with SSSRs, and are followed by efficient suppression of the S100A8/A9-mediated lung tropic metastasis *in vivo*.