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MSC-based therapies for the treatment of cancer

Pancreatic Cancer UK Discovery and Translational Research Forum 2022
Dr Andrea Mohr

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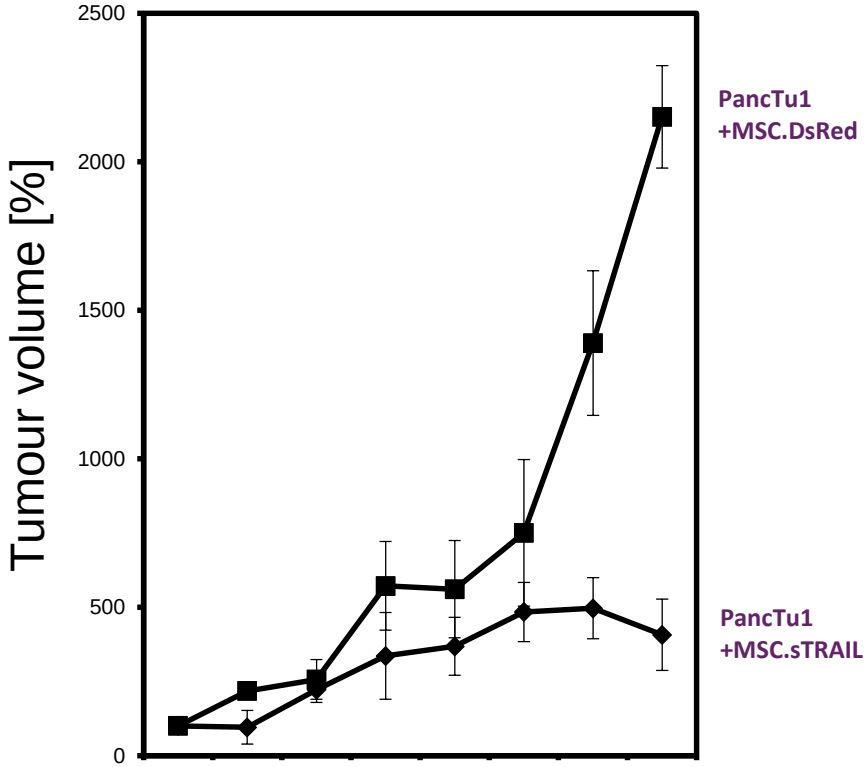
Development of an MSC-based therapy for the treatment of pancreatic cancer



Model	Metastasis	Metastasis induced/ enhanced by mMSCs	by hMSCs
Breast Cancer (MDA)	+	+++	+++
Breast Cancer (4T1)	+++	+++	n/d
Colon Cancer (HCT116)	-	++	n/d
Pancreatic cancer (PancTU1)	-	+++	n/d

MSC-mediated tumour progression is tumour type independent and also independent from the species the MSCs were isolated from

9 clinical trials using MSCs for the treatment of cancer

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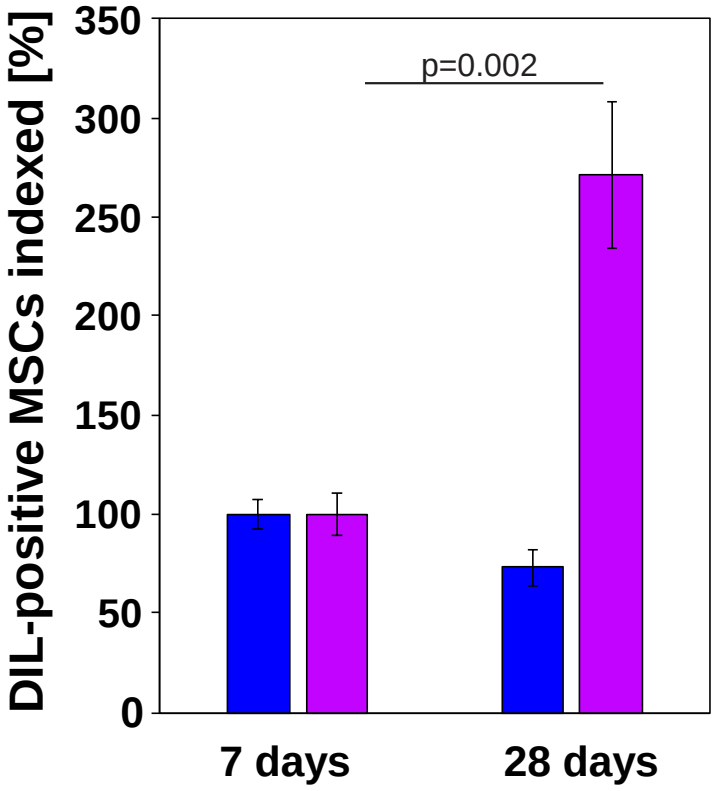
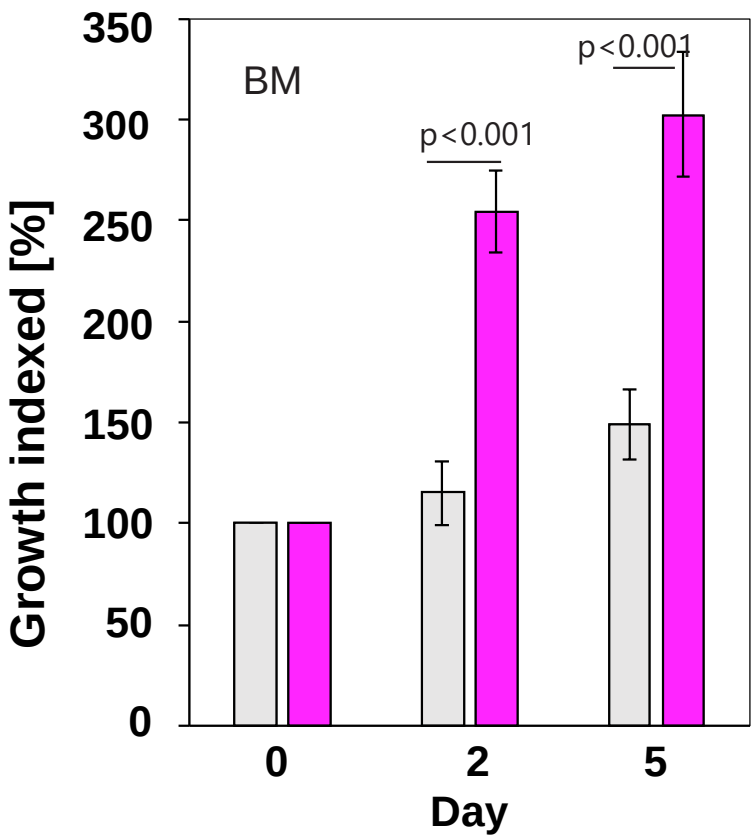
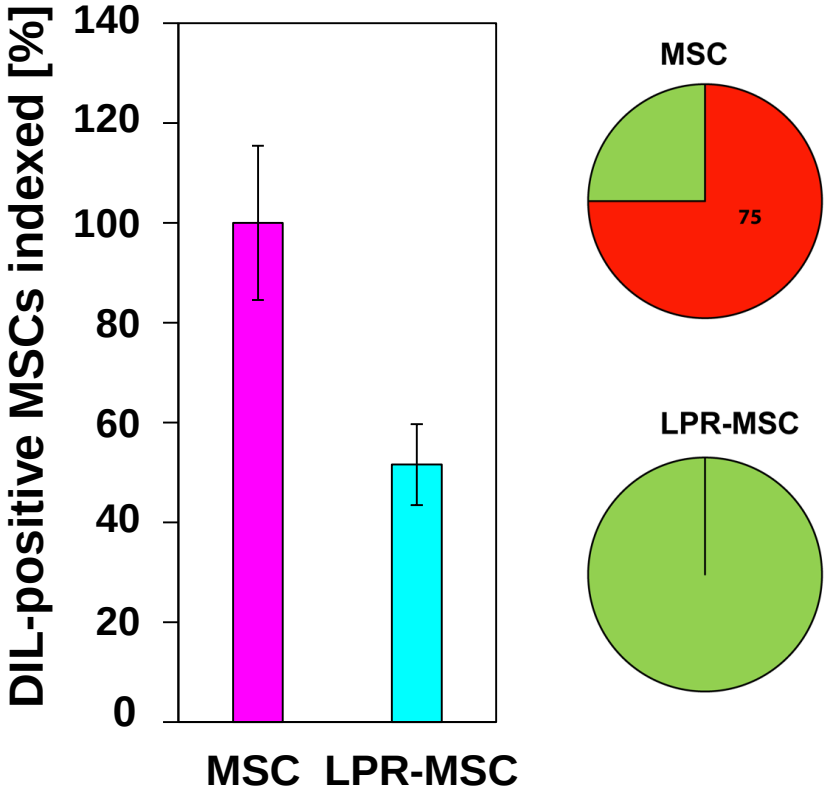
MSCs proliferate in response to FasL



MSCs proliferate in tumour burden animals



MSCs proliferate in response to low-level FasL signalling



LPR-MSCs do not proliferate in tumour bearing animals and do not induce metastasis

FasL/Fas signaling → higher numbers of MSCs → higher pro-metastatic activity arising from MSCs

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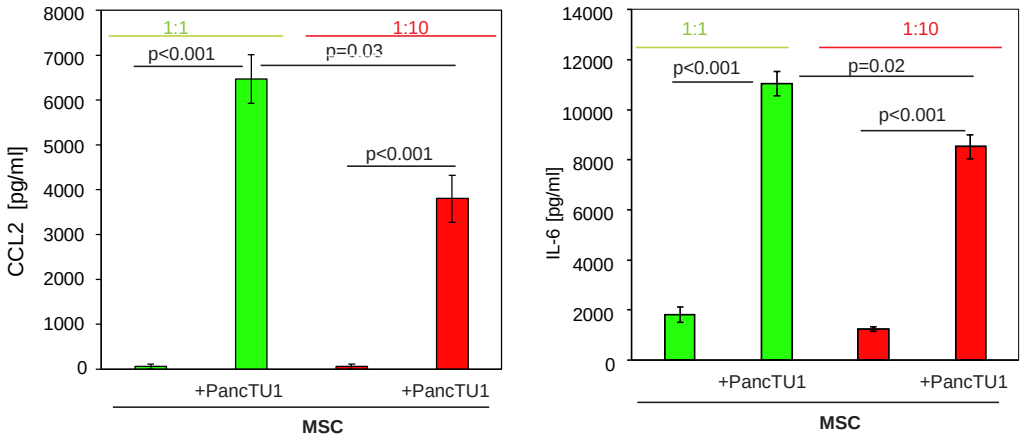
The amount of CCL2 and IL-6 secreted is dependent on the number of MSCs

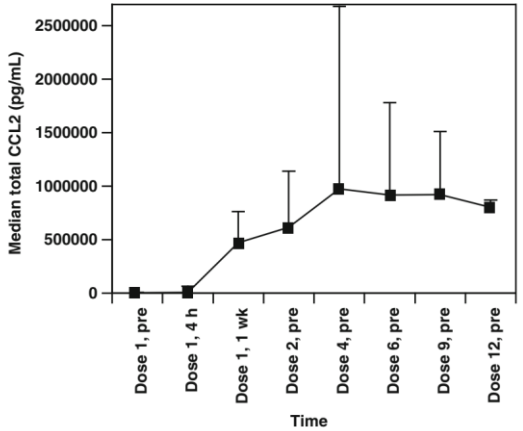


The more MSCs were mixed with tumour cells, the more cytokines were produced by MSCs

Elevated levels of CCL2 have been correlated with disease progression

CCL2i in clinical trials:

- CCL2 levels were initially suppressed following treatment
- CCL2 concentration quickly increased,
- surpassing pre-treatment serum concentration, and
- elevated levels were sustained even after subsequent CCL2i administration



(Pienta et al. Invest New Drugs 2013;3:760-8)

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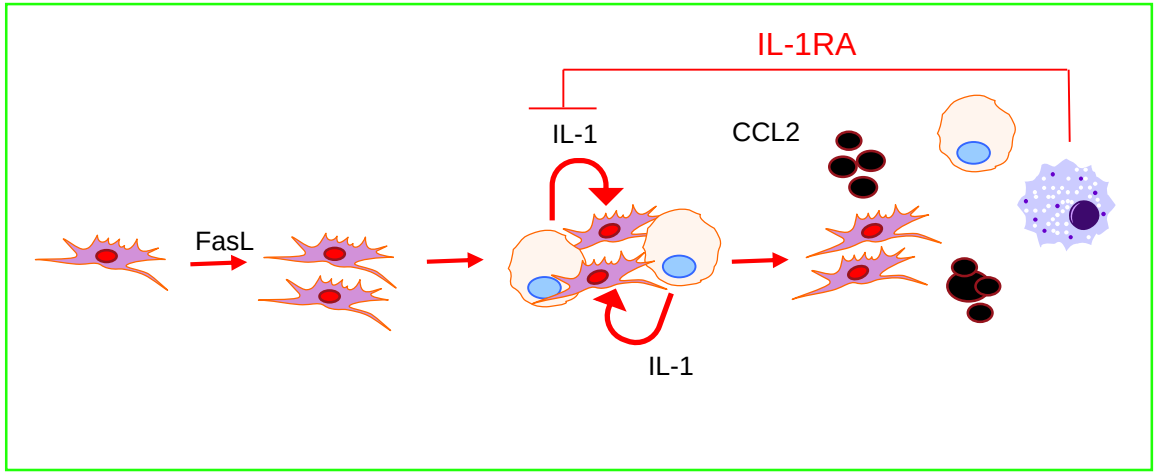
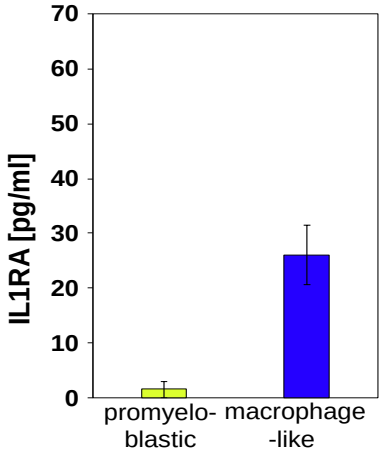
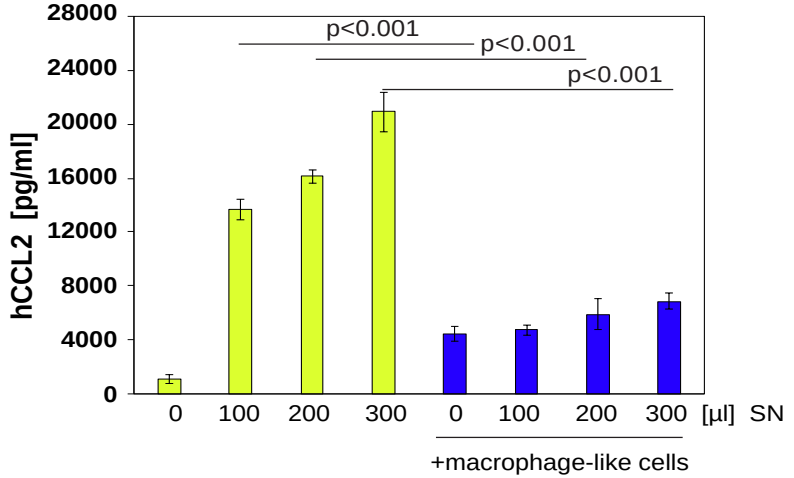
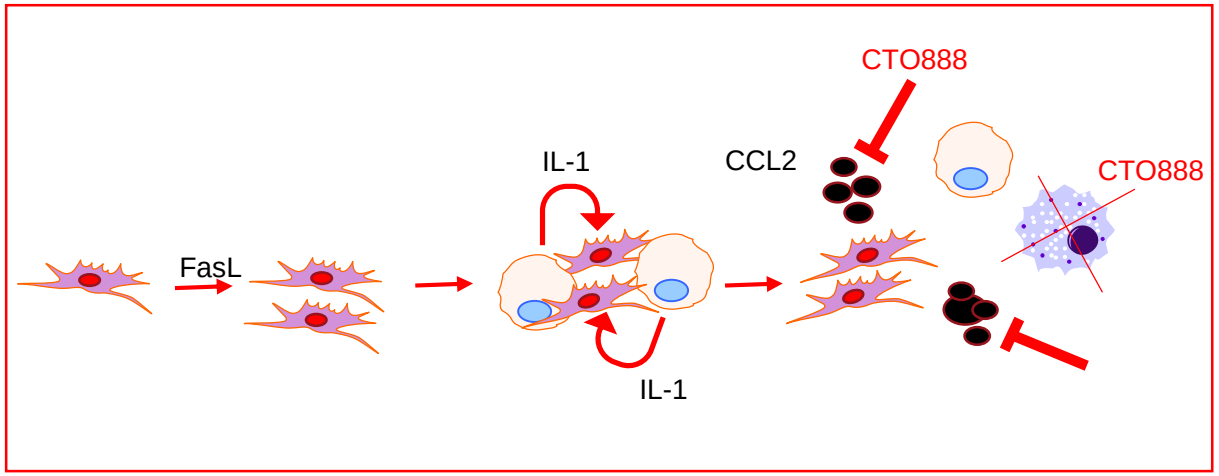
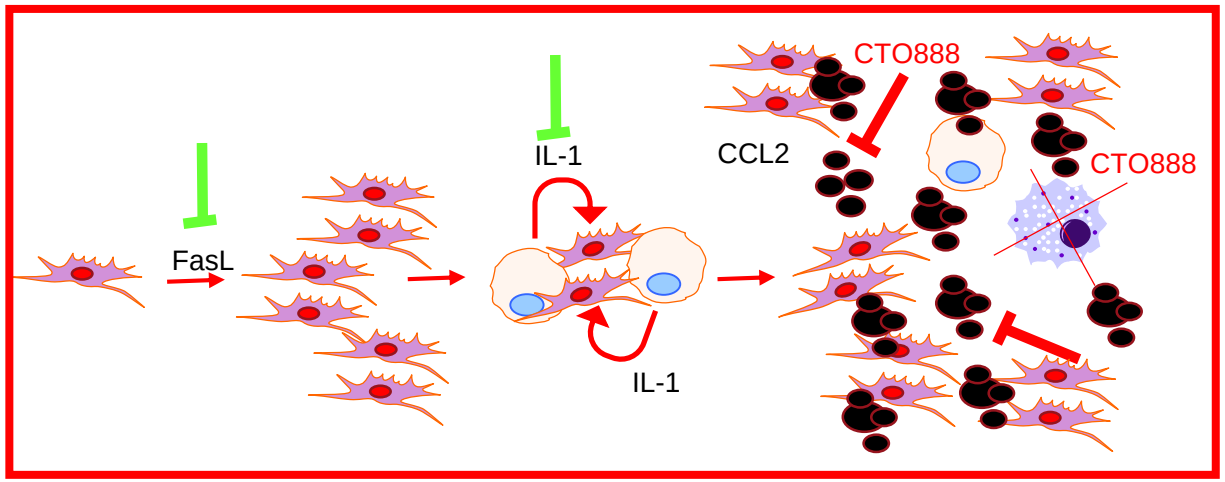
Potential immediate clinical implications











MSCs are continuously proliferating and secreting CCL2

CCL2 cannot be scavenged any longer

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