Breast Cancer Cells and Macrophages in a Paracrine-Juxtacrine Loop

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Background

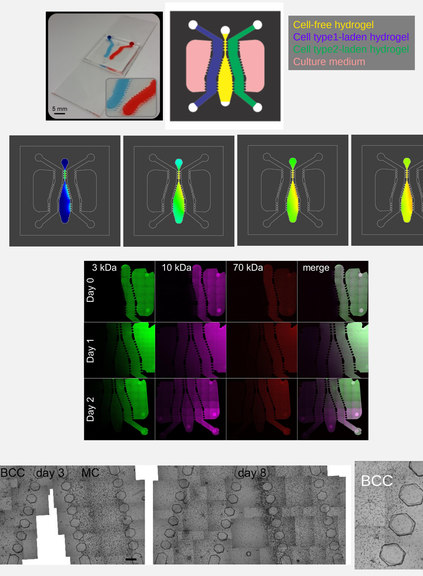
Macrophages have been shown to promote invasion and change multicellular organization of cancer cells. Breast cancer cells (BCC) and macrophages (MC) are known to interact via epidermal growth factor (EGF) produced by macrophages and colony stimulating factor-1 (CSF-1) produced by BCC.

Knowledge gap

Despite contradictory findings, this interaction is perceived as a paracrine loop. Yet, an in-depth understanding of the mechanistic basis of this interaction is lacking: It is not known whether the interactions between breast cancer cells and macrophages are based on chemotaxis or haptotaxis or direct contact.

Results

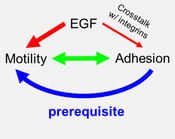
BCC cells did not show chemotaxis towards macrophages whereas macrophages showed chemotaxis towards BCC.



CSF-1 but not EGF was secreted.

EGF / Total protein in conditioned medium = 0.012 pg/mg
CSF-1 / Total protein in conditioned medium = 15.111 pg/mg

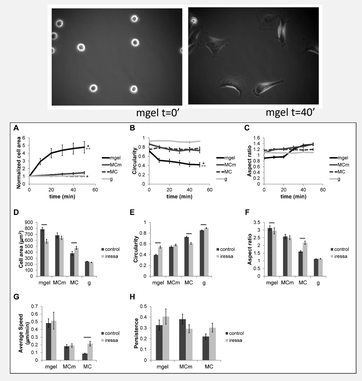
EGF – motility – *adhesion*



If cells are adherent, EGF can enhance adhesion via crosstalk with integrins.
➔ *iressa can reduce enhanced adhesion.*

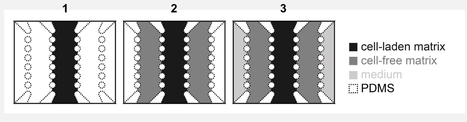
If cells are not adherent, EGF still provides pro-motility signal.
➔ *iressa can reduce EGF signaling allowing cells to adhere better.*
➔ *iressa can increase motility because the prerequisite of adhesion is satisfied.*

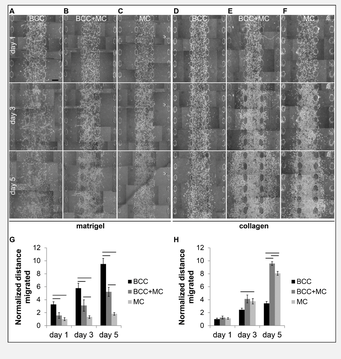
MC and MCm did not support initial cell attachment as well as matrigel.
MC but not MCm modulated adhesion of BCC in an EGF-dependent manner.



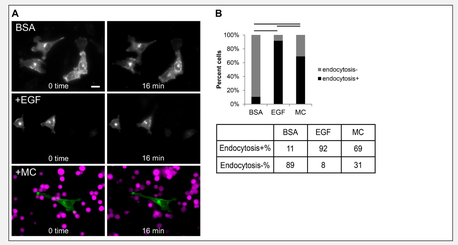
mgel : Matrigel, MCm: Macrophage derived matrix, MC: Macrophages, g: Glass

Macrophages reduced and promoted migration of BCC in matrigel and collagen, respectively.





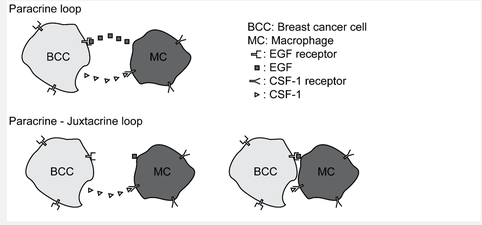
Adherent BCC endocytosed EGFR when in contact with macrophages.



	BSA	EGF	MC
Endocytosis+%	11	92	69
Endocytosis-%	89	8	31

Conclusions

Collectively, our data revealed that macrophages showed chemotaxis towards BCC-derived-CSF-1 whereas BCC required direct contact to interact with macrophage-derived-EGF. We propose that the interaction between cancer cells and macrophages is a paracrine-juxtacrine loop of CSF-1 and EGF, respectively.



References and acknowledgements

References: Goswami S et al., Cancer Res., 2005, 65, 5278-83; Vlaicu P et al., BMC Cancer, 2013, 65, 5278-83; Comoglio et al., 2003; Eliceiri et al., 2001; Kim et al., 2008; Yamada et al., 2002; Welsh et al., 1991; Maheshwari et al., 1999; Xie et al., 1998; Bai et al., 2015; Goswami et al., 2005; Needham et al., 2016; Philippar et al., 2008; Verveer et al., 2000; D. Pesen Okvur, US Patent 9,815,059.
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