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## Chemokines in Ewing sarcoma

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# Stellingen

Behorende bij het proefschrift

## Chemokines in Ewing sarcoma

1. Inhibitory factors of CXCR4 activation, CXCR7, CXCL14 and ratio between CXCR-1 and CXCR4-2 splice variants are prognostic markers for survival in Ewing sarcoma (*This thesis*)
2. There are four splice variants of CXCR4 observed and this alternative splicing might influence the CXCR4 ligand binding efficacy at the N-terminal domain (*This thesis*).
3. CCL21 RNA expression levels can be used as a prognostic factor in Ewing sarcoma, implying the importance of the immune component of the tumor microenvironment of Ewing sarcoma (*This thesis*).
4. CCL21 activation immunotherapy might have a large potency in Ewing sarcoma patients with low CCL21 expression and no CCR7 expression (*This thesis*).
5. Fluorescently labeled T140 CXCR4 targeting peptide-based method enables qualitative and quantitative studies on CXCR4 both *in vitro* and *in vivo*. (*This thesis*)
6. Studying CXCR4 dynamics in life cells is enabled by using an activatable CXCR4 endocytosis tracer, based on FRET dimer coupled to a receptor targeting peptide (*This thesis*).
7. “Tumor microenvironments and key signaling pathways are broadly diverse between different tumor types and tissues, insights into how to manage this diversity and how different tumor microenvironments may alter response to current standard-of-care therapies will be important areas to investigate going forward” (Quail and Joyce, *Nature Medicine* **2013**, 19, 1423-1437).
8. EWS-ETS oncogenic fusion orchestrates both epigenome and transcriptome rewiring at a large extend (Tomazou *et al.*, *Cell Reports*, **2015**, 10, 1082-95)
9. “It is being recognized that chemokines and their receptors serve as critical communication bridges between tumor cells and stromal cells to create a permissive microenvironment for tumor growth and metastasis”. (Guo *et al.*, *Oncogene*, **2015**)
10. “The activity of CXCL12 is controlled and fine-tuned by glycosaminoglycans (GAGs), which sequester and present CXCL12 to CXCR4” (Hoellenriegel *et al.*, *Blood* **2014**; 123, 1032-1039)
11. The roles of CXCR4 signaling in certain physiological or pathophysiological settings may be very complex; depending on the cell type, microenvironment, and perhaps

potentially inter-individual settings (Pawig et al. *Frontiers in Immunology*, **2015**, *6*, 429)

- 12.** The context is the key to translation
- 13.** You can't depend on your eyes when your imagination is out of focus. (Mark Twain, "*A Connecticut Yankee in King Arthur's Court*", **1889**)
- 14.** Leren zwemmen is een ding maar in rechte banen zwemmen is een tweede.