Immune cell complexity in the tumor microenvironment of breast cancer

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Stellingen behorend bij het proefschrift getiteld "Immune cell complexity in the tumor microenvironment of breast cancer"

1) Tumor-associated macrophages are heterogeneous populations that differ between tumor types. As they can affect tumor progression and therapy response, understanding the drivers and consequences of their phenotype will reveal important aspects of cancer biology (this thesis)

2) The M1/M2 dichotomy to define tumor-associated macrophages is too simplistic to interpret the complexity of macrophage phenotype. Indeed, macrophages can express both M1 and M2 specific genes in human cancer (Azizi et al. Cell 2018, Singhal et al. Sci Transl Med 2019)

3) The future of macrophage-targeting drugs for the treatment of cancer will rely on strategies able to re-educate macrophages rather than depleting them (Kowal et al. Immunotherapy 2019)

4) Besides depleting the majority of tumor-associated macrophages in the K14cre;Ecad$^{F/F}$;Trp53$^{F/F}$ mouse model for breast cancer, anti-CSF-1R induces type I interferon production from an intratumoral population of macrophage-like cells. Understanding the molecular mechanisms leading to this phenotype change is critical to develop new therapeutic strategies that could synergize with chemotherapy treatment (this thesis)

5) Although its role is generally considered beneficial both during infection and in cancer, type I interferon can also induce negative feedback and immunosuppression (Snell et al. Trends in immunology 2017)

6) The study of neutrophils in cancer has been hampered by the lack of efficient strategies to deplete these cells (this thesis)

7) Due to its plasticity and versatility, the immune system can induce resistance mechanisms to the effects of immunomodulatory drugs via inflammatory signals (Nywening wt al. Gut 2018, Pahler et al. Neoplasia 2008, Rivera et al. Cell rep 2015, Swierczak et al. Cancer Immunol Res 2014)

8) Chemotherapeutic agents can elicit immunomodulatory effects that can impact the clinical outcome of immunotherapy (this thesis)

9) "Everything must be taken into account. If the fact will not fit the theory—let the theory go" (Agatha Christie, The Mysterious Affair at Styles, 1920). Similarly, scientists should always prioritize evidence over expectations.

10) “Science, my boy, is made up of mistakes, but they are mistakes which it is useful to make, because they lead little by little to the truth” (Jules Verne, Journey to the Center of the Earth, 1864). Every discovery is the result of several failed attempts.