Macrophages in colorectal cancer: proof of principle for diagnostic application

1.3 Monitoring relevance

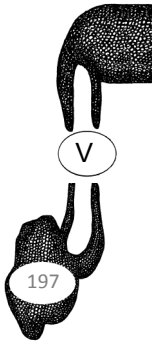
Monitoring response to neoadjuvant treatment in rectal cancer patients could enable identification of responders and non-responders before or early during neoadjuvant therapy[7]. In combination with blood biomarkers this additional value was reported in a prediction model utilised before neoadjuvant treatment[8]. In our studies it was shown that the added value could be increased even further (AUC 0.94), by adding monocyte and macrophage analyses in combination with other serum markers and PET-CT values to a prediction model during the first two weeks of neoadjuvant treatment. When evaluating these outcomes upfront in all rectal cancer patients, the patients benefitting from neoadjuvant treatment could be identified. The patients who would not benefit could be treated according to other protocols or specific patients could refrain from therapy at all. These emerging options would lead to personalised medicine, that could lead to better quality of life for rectal cancer patients, and more appropriate spending of resources.

2. Target groups, activities and products

The medical specialities who could utilise the outcomes of this thesis arethe gastroenterologists and surgeons treating CRC patients. Immunologists could utilise the outcomes to further investigate the role of macrophages and monocytes in immunocompetence in cancer in general and specifically in CRC. When proven useful, development of an immuno-competence assay for cancer patients could be the next step. Oncologists could incorporate immunological assays (such as the EDIM-assay) in cancer follow-up settings for disease monitoring purposes. Finally, Radiotherapists could first investigate and at a later time point include monocyte and macrophage measurements, utilising the EDIM method, in treatment monitoring settings. National and global funding organisations should recognise the potential of immunological cancer research and expand their funding capacity towards this part of medical research. Participation of other (UM-) parties in further development of this assay could accelerate the development and broaden the applicability in medicine.

3. Innovation

The EDIM-method is a completely new way of utilising cells of the immune system, such as monocytes and macrophages, for diagnostic, follow-up and



monitoring purposes. In prostate cancer this method was first described for diagnostic purposes by Herwig et al.[9-12] and confirmed by Leers et al. in 2008[13]. The basic question of the actual localisation of tumour markers in macrophages was investigated by our group using the colorectal cancer model. Utilising light and electron microscopy the localisation of the antibody against CEA inside the monocytes and macrophages was visualised and confirmed[14,15]. In a pilot setting this innovative method was applied in a CRC diagnostic setting showing distinguishing capabilities between healthy and CRC patients. Addition of CRP allowed distinguishing CRC patients from benign inflammatory diseases of the colon[16]. Validation of such an assay is innovative. All parts of the validation process must be conceived, tested and applied. This process has been performed and reported by our group[17]. The potential of applying the assay in CRC follow-up (research in progress) and in monitoring rectal cancer (paper submitted) has been and is currently being explored by our research group. The value of the EDIM-method in comparison to established diagnostic tools and other experimental methods in cancer diagnostics needs further evaluation.

4. Planning and realisation

Studies as described above are currently performed or have been performed with the results being published soon.

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