Comparison of chemosensitivity testing of CETCs and spheroids in cancer patients with solid tumors

Background: In vitro chemosensitivity testing of circulating epithelial tumor cells (CETCs) provides real-time information about the sensitivity of the tumor cells present in the patient and correlates with treatment success. Nonetheless, a fraction of CETCs can survive after conventional chemotherapy and grow into distant metastases. A subpopulation of CETCs with proliferation activity has the ability to form spheroids in suspension culture. Spheroids exhibit stem-like cellular properties and might require alternative therapeutic strategies. Therefore, the aim of our study was to compare the efficacy of chemotherapeutics in disrupting the spheroids originating from the same individuals.

Methods: The proliferation of CETCs isolated from patients with solid tumors in clinical stage I-IV were used in the antiEpCAM treatment method. Subsequently, viable CETCs were cultured in a suspension culture system allowing for spheroid formation. To evaluate the cytotoxic effect, CETCs and spheroids in short time cultures were exposed to different concentrations of anticancer drugs for different periods of time.

Results: The response to chemotherapeutics was different in CETCs and spheroids. In contrast to CETCs, spheroids from the same patients were significantly more chemoresistant. Whereas active drugs led to tumorsphere destruction in single CETCs and subsequent disintegration of the nucleus with propidium iodide, the same drugs led to a disintegration of spheromeres with destruction of part of the cells but often part of the cells in the spheres was able to survive. Furthermore, and especially salinomycin, a polyether saponin antibiotic isolated from Streptomyces albus showed the best effects. Additionally, cytospin preparations and 5-fluorouracil showed almost no cytotoxic effects onto the cells in the spheres.

Conclusion: Our results show, for the first time that stem cells circulating in peripheral blood, capable of forming spheroids are more resistant to anticancer drugs than the remnant circulating cancer cells. On the other hand, it is clear that salinomycin efficiently destroys spheroids cultured from CETCs, strengthening its role as a promising anti-cancer therapeutic.