Editorial

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The emerging role of chemosensitivity and resistance testing in malignant effusions

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Testing tumor cells *ex vivo* and subsequently instituting an individualized antineoplastic chemotherapy has been the focus of intense research for decades [1]. Chemosensitivity and resistance testing has an enormous potential to reduce the use of unnecessary chemotherapies and the side effects associated with these therapies, to improve the efficacy of cancer treatments, and to substantially reduce health care costs. Until now, however, the dream of simply and quickly testing the tumor's sensitivity before choosing the most effective chemotherapy has not come true. This may be somewhat surprising because this intuitive concept works very well in other areas of medicine, e. g. antibiotic treatment of infections. The reasons why it is so difficult to develop reliable and representative individual tumor models, are not clear, but – most likely – it is a whole range of issues making chemosensitivity and resistance testing so difficult. Apart from tissue availability and quality, it is tumor heterogeneity and tumor polyclonality both within individual tumor nodes and between different tumor metastases, that makes it very difficult to adequately sample a tumor in a way that is representative for the rest of the malignant tissue. Also, tumors intensively interact with their environment and *vice versa* and the influence of the environment on the tumor is considerable [2]. This influence of the tumor environment is variable depending on the site of the tumor, for example, the lung, liver, and peritoneum. If metastatic tumors are present in all of these locations, a tissue specimen from the liver may not be necessarily representative of malignant tissue in the lung. This problem is not only true for the metastatic situation, but also for the primary situation, where many tumors have already spread to the regional lymph node environment and bone marrow. Lastly, sampling tumor tissue where it is readily available does not touch on the problem of tumor stem cells. Tumor stem cells are typically not easily accessable and if it is true that they determine the fate of the patient, testing peripheral tumor tissue might not be successful in the long-term.

These issues demonstrate how great the obstacles are for chemosensitivity and resistance testing. However, the potential usefulness of this method is so great, that further research in this area is of great clinical importance. Therefore, we are happy to introduce a thorough review of chemosensitivity and resistance testing by Szulkin et al. in this issue of *Pleura and Peritoneum* [3]. The authors summarize the up-to-date methods of measuring chemosensitivity and resistance such as clonogenic assays, fluorescence activated cell sorting (FACS), and viability testing by confocal microscopy, a method developed by the authors. Most importantly, this review focusses on malignant effusions as cellular tumor models for chemosensitivity and resistance testing. This is an innovative approach with many advantages, among them availability and easy accessibility, and a biology which is representative of the primary tumor's characteristics. The authors present data demonstrating that malignant effusions in the form of primary cells, short-term cultures, and even xenografts have an emerging role as valid models for chemosensitivity and resistance testing. Pointing to the future, the authors also present and discuss evidence on genome wide screening of tumor tissue and pleural effusions. Tumor-specific chemoresistance gene signatures may be a way forward in the fine-tuning of this area of research. In the end, however, clinical trials comparing treatment strategies with empirical drug choice versus drug choice based on chemosensitivity testing will decide the clinical usefulness and applicability of this approach. To date, these trials are not available, but the tools – as evidenced by Szulkin et al. – are readily available to make the next step.

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