Method and kit for the ex vivo evaluation of the response of a tumor to conditions to be tested

Project: 17009

Background /Medical Problem
Biomarkers for the reliable prediction of a response of a malignant tumor to chemotherapy including targeted therapies and immunecheckpoint inhibitors (e.g. PD-1, PD-L1) and hence a successful treatment are missing. This is especially the case in a number of solid cancers, including head and neck cancer and others. The patented invention concerns a method and kit for the ex vivo evaluation of the response of a tumor to conditions to be tested, in particular a tumor treatment regime, in an isolated tumor sample. The diagnostic method is suitable for the use in medicine and in pharmacy, in particular for the pre-therapeutical evaluation of the responsiveness of a tumor to a tumor treatment regime and the preclinical evaluation of a tumor treatment regime. The invention overcomes a number of limitations in conventional in vitro analyses by sound approach avoiding in particular photoactivation and unwanted chemical reactions of the compounds to be tested with components of cell culture medium.

Technology /Solution
The method comprises:

a) Placing a freshly isolated tumor sample in a container, which contains antibiotics and preferably antimycotics keeping the sample at a temperature above 10 °C,
b) Breaking up, preferably mechanically disintegrating, the tumor sample,
c) Placing the pieces of the tumor sample into cell culture medium and incubating with collagenase IV shortly upon isolation of the tumor,
d) Plating the cells and tissue pieces into wells that are coated with extra cellular matrix components, incubating under the conditions of the tumor treatment regime or in presence of a substance and mixture of substances to be tested,
e) Determining the number of cells and/or the number of colonies and/or the sum response of cells of epithelial origin, preferably by performing a cytokeratin staining,
f) Using a cell culture medium in the steps c.) to e.) that contains less than 100 nmol/l flavin and that does not contain phenol red,
g) Performing the steps c.) to e.) in the absence of light of a wavelength below 520 nm.

Further reading:

Fig.: Main features of patent EP 2 271 935 B1

Benefits
Pretherapeutical evaluation of combinations or series of tumor treatment regimes using in vivo tolerable concentrations of therapeutics: not only proof of principle!
-> reliable reflection of response or chemoresistance of the tumor
-> targeted therapy strategy within 3 to 7 days
-> results reflect the in vivo situation

Potential Application
Testing of response of a tumor to a chemotherapy scheme
Drug screening
**Method and kit for the ex vivo evaluation of the response of a tumor to conditions to be tested**

**Development Status**

- **Idea**
  - Testing the responsiveness/resistance of a malignant tumor ex vivo with the chemotherapeutics in concentrations reflecting the in-vivo situation

- **Demonstrator**
  - Along the DeLOS-II phase II clinical trial, the invention revealed a positive predictive value for response of 89.5%

- **Prototype**
  - The method according to the method of the invention is established in the ENT Research laboratory of the Clinic of Otolaryngology, Head and Neck Surgery and used routinely

- **Series Production**
  - ... potentially in the context of companion diagnostics

**Intellectual Property Rights**

- EP2271935 (B1), WO2009124997 (A1)
- IL208524 (A)

**Cooperation Options**

- License Agreement
- R&D Agreement
- Ownership Agreement

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