Oncology pharmacy activities in the Czech Republic

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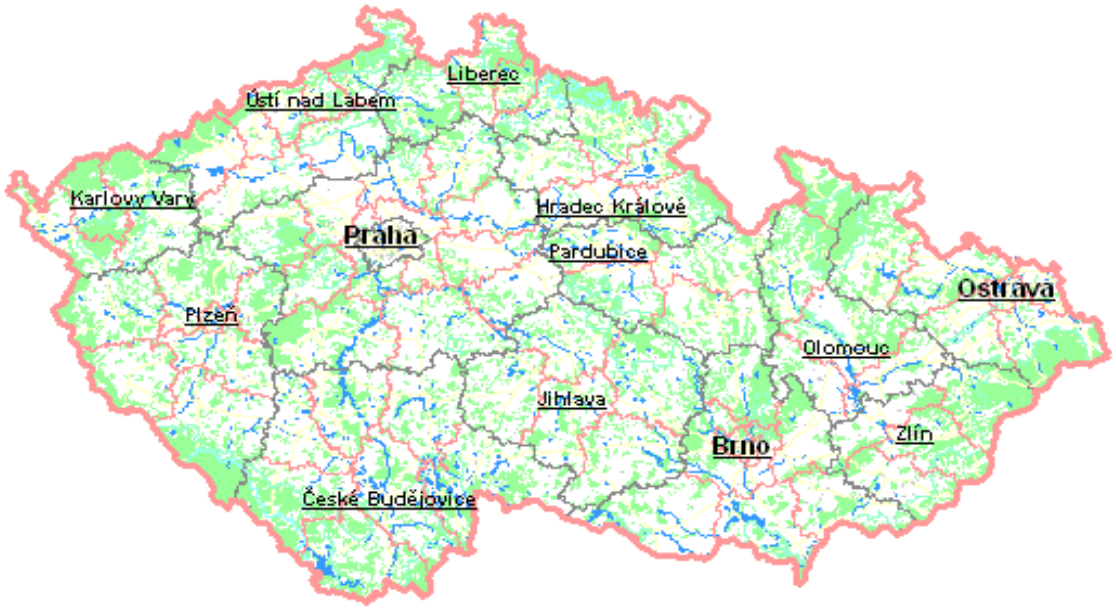
The Czech Republic



History

- In the 90s the **first central department** for cytotoxic preparations was established in Brno in the Masaryk Memorial Institute.
- On May the 5 th 2004 **the Oncology Pharmacy Working Group** was established as a part of the Czech Pharmaceutical Society JEP.

Present situation

- 6 hospitals with special facilities for cyto-preparations in the hospital pharmacies
- 6 other hospitals are planning to provide centralised cyto-preparation facilities
- The Oncology Pharmacy Working Group has 35 members

The Masaryk Memorial Institute

- The oncological centre with full range of services
- 230 beds
- Major centre for oncology pharmacy training

First central department for cytotoxic preparations in the MMI Brno

SPFO Congress, Cannes 2005

Teaching Hospital Bulovka

- Second established department for cytotoxic preparations
- In the year 2000

Teaching Hospital Ostrava

Thomayer Memorial Hospital Prague

The future new cyto-department

Oncology Pharmacy Working Group

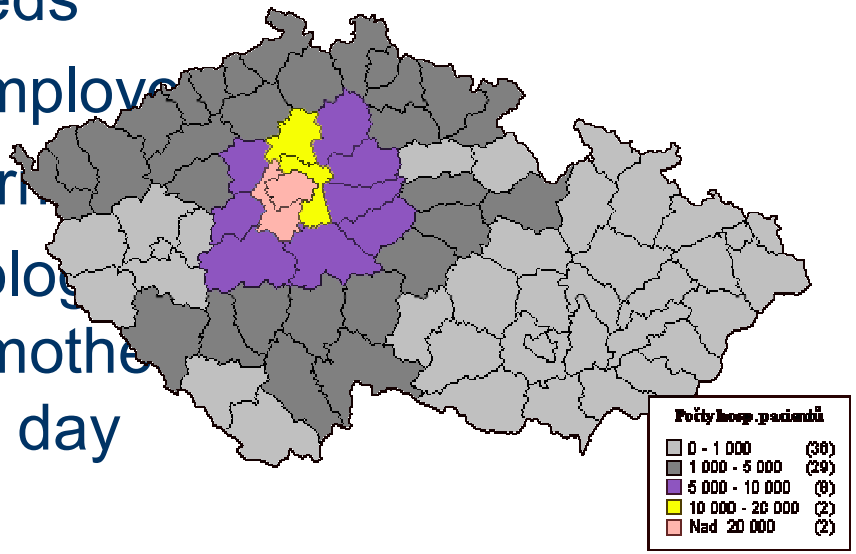
- to provide education activities for pharmacist and technicians twice a year in area CPD
- to organize postgraduate study for pharmacists
- to liaise with insurance companies, the Ministry of Health and other professional societies
- to support research in the field of oncology pharmacy
- to develop the clinical part of oncology pharmacy

General Teaching Hospital Prague

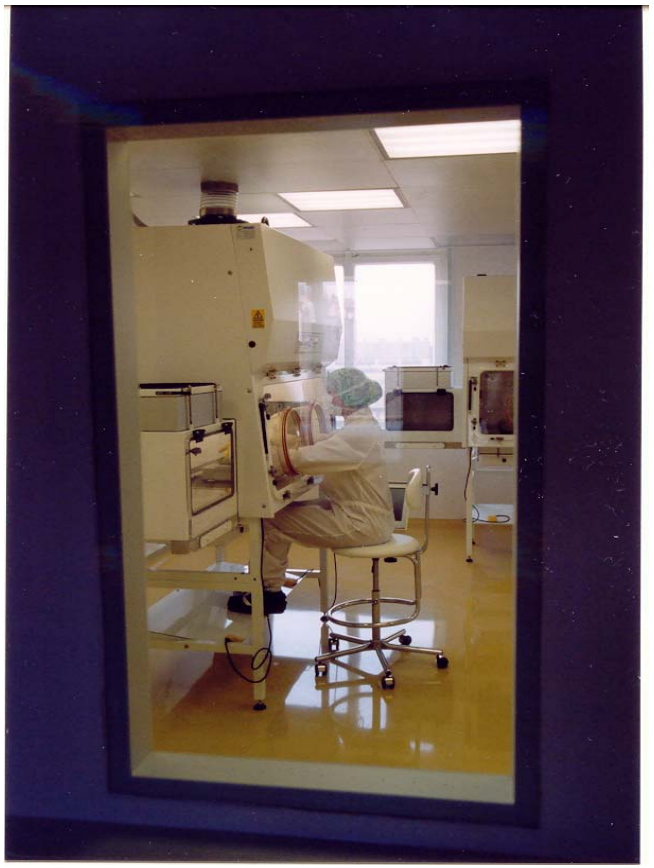
GTH Prague – the building of Oncological Clinic

GTH Prague

- 1767 beds
- 4340 employe
  (25 phari
- 80 oncolog
  for chemothe
  working day



Cyto – department, GTH Prague



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- Hospital pharmacy staff are keen to further develop their professional skills and provide **clinical pharmacy** in oncology wards.
- Cooperation with the Faculty of Pharmacy and the Ist Medical Faculty of the Charles University in the **research area.**
- Pharmacists are engaged in:

  a/ chemoresistance testing

  b/ pharmacogenetic studies in oncolgy

Clinical pharmacy activities in the Hematological Clinic of GTH Prague

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Chemoensitivity/chemoresistance testing

Chemotherapy:

- basic systemic treatment of malignant disease
- based on staging (TNM)
- randomised clinical studies

Reason of different responses to chosen chemotherapy schemes

Heterogenity of biological properties

in the tumor cell population

- ✓ in one histological tumor type
- ✓ in particular patients

Primary chemoresistance

- Tumor cells of the particular histopathological cancer are not sensitive to one or more particular cytotoxic drugs

  e.g. breast carcinoma and aktinomycin D
- Tumor cells from particular patient are not sensitive to cytotoxic drug usually used in treatment

Secondary chemoresistance

- Tumor cells sensitivity decreases during treatment
- **Cross resistance** – loss of sensitivity to similar cytotoxic drugs
- **Multiple drug resistance** – loss of sensitivity to cytotoxic drugs with different structures and effects

Chemoresistance is influenced by:

- Changes in drug metabolism
- Drug penetration into the tumor
- Intracellular uptake
- Intracellular interaction with target structures
- Changes in cell signal paths

Pharmacokinetic changes

- Decreased drug absorption
- Faster drug biotransformation
- Faster drug elimination

Cytokinetic changes

- Changes in the G_0 phase
- With increased number of tumor cells is increasing the number of spontaneous mutations, heterogenity of cell population and changes in chemosensitivity
- Non functional cell cycle self regulation

Structural and functional changes in cells

- Changes in activity of cell enzymes
- Disturbance of intracellular distribution of cytotoxic drug (e.g. binding to lysosom)
- Influence of cytotoxic drug transport through cell membranes
- Increased DNA repairs

Molecular mechanism of drug resistance

- **Typical multidrug resistance (MDR)**

  P-glykoprotein
- **Atypical multidrug resistance**

  MRP, LRP, GST, alkyltransferases
- **Other mechanisms**: thymidilatsyntetases, dihydrofolatreductases, protein p53, topoisomerases I and II

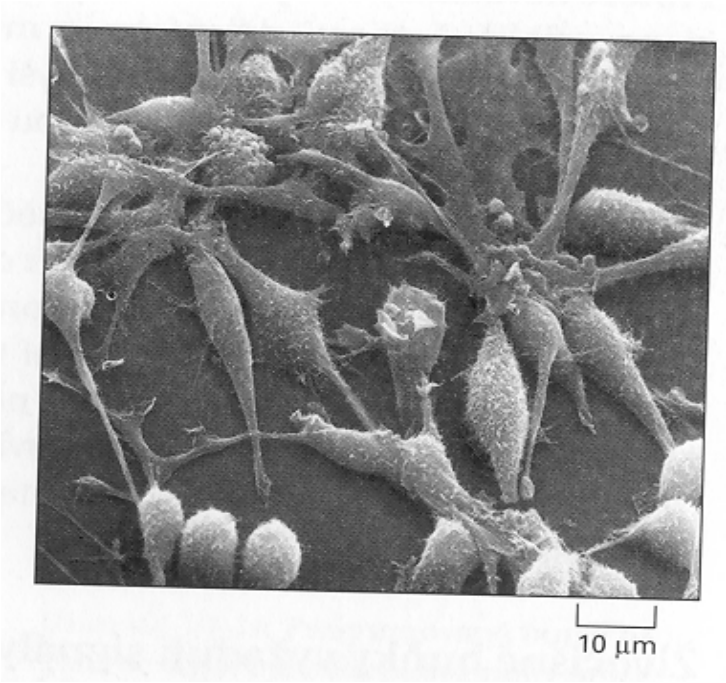
The Laboratory of Tumor Biology
I.Medical Faculty of the Charles University

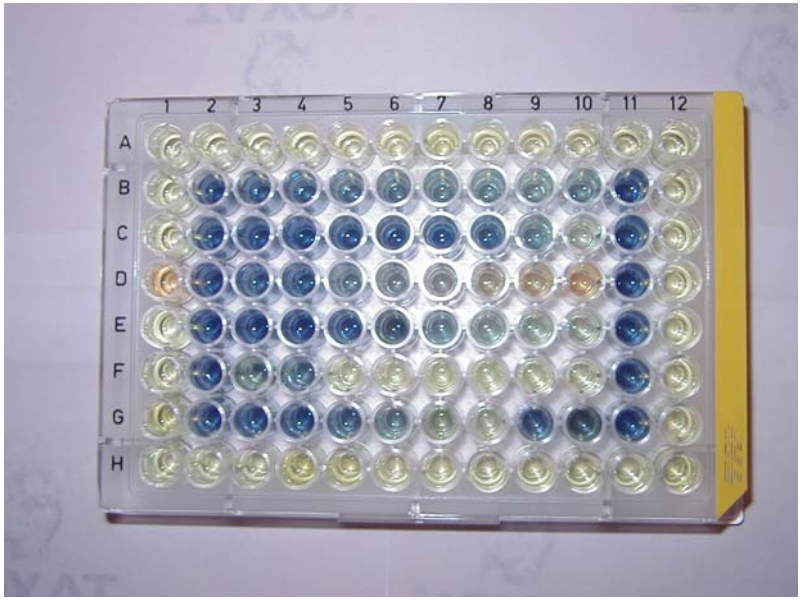
- We perform **chemoresistance assays** with the aim of identifying *in vitro* ineffective cytotoxic drugs and thus improve the chemotherapy plan and its results for advanced cancer patients.
- The main task of our research is to find how to connect the chemoresistance found in in vitro assays with the effect on the tumor.
- This direction of research appears to make a valuable contribution to the individual tailoring of the therapy for oncological patients.

MTT assay

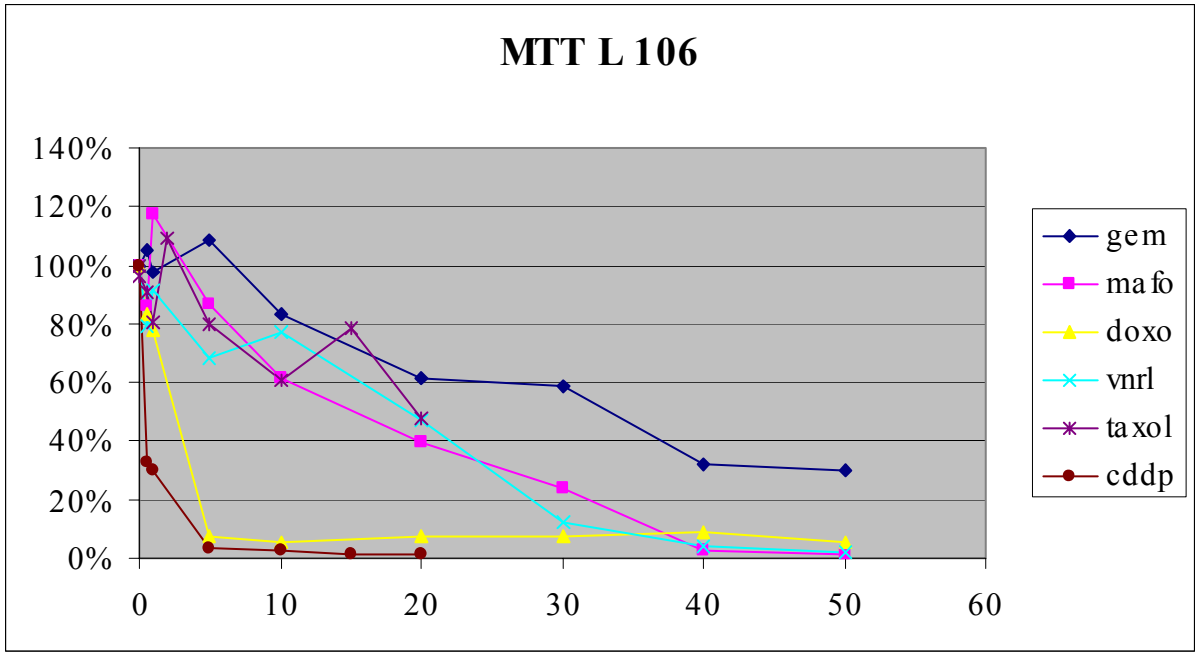
- After this „treatment“, viability of cells is determined by MTT assay.
- If the cancer cells are able to survive under these conditions, there is high probability that they will also be able to proliferate in the human body.
- MTT assay is based on mitochondrial Krebs cycle activity measurement.

In vitro chemoresistance testing: MTT assay





MTT assay – graph



Thank you for attention