UNIVERSITÉ DE GENÈVE
FACULTÉ DES SCIENCES
Section des sciences pharmaceutiques

Ecole de Pharmacie EPGL Genève – Lausanne

Master en pharmacie:

Travail personnel de recherche
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Search for optimal drug combinations for cancer treatment

Unité de rattachement:	Molecular Pharmacology Group	N° du sujet:
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Lieu des travaux:	CMU	
Conditions particulières		

PRÉSENTATION DU PROJET

The use of targeted therapies is currently a widely implemented approach for cancer therapy. The actual contribution of these agents to the prolongation of overall patient survival, however, is still rather limited due to genetic heterogeneity and the development of drug resistance (*1*). A major improvement in therapeutic outcome may be achieved by optimally combining these drugs. We have recently developed and validated the feedback system control technique (*2*), a mathematically-based strategy, to search for optimal drug combinations (ODC). The strength of this methodology lies in a possibility of a rapid drug optimization towards selected cell type or selected mutation with a minimal experimental effort (*3*). The scope of this project will be the identification of the cell death mechanism after treatment of the ODCs, in the parental and a drug-resistant cell lines.

PARTIE EXPERIMENTALE

The candidate will firstly perform a literature search on the known cell death mechanisms for the individual drugs present in tested ODC. The laboratory work will work will be performed both in 2D and 3D cell culture models with the use of flow cytometry. The candidate will measure cell faith (the level of apoptosis, necrosis) and the cell cycle regulation. If time allows the candidate will test the ODC in the preclinical tumor model (the chicken chorioallantoic membrane model, CAM) (*4*).

RÉFÉRENCES

1. J. R. van Beijnum, P. Nowak-Sliwinska, E. J. Huijbers, V. L. Thijssen, A. W. Griffioen, The great escape; the hallmarks of resistance to anti-angiogenic therapy. *Pharmacol Rev* **67**, 441 (2015).
2. P. Nowak-Sliwinska *et al.*, Optimization of drug combinations using Feedback System Control. *Nature protocols* **11**, 302 (Feb, 2016).
3. A. Weiss *et al.*, A streamlined search technology for identification of synergistic drug combinations. *Scientific reports* **5**, 14508 (2015).
4. P. Nowak-Sliwinska, T. Segura, M. L. Iruela-Arispe, The chicken chorioallantoic membrane model in biology, medicine and bioengineering. *Angiogenesis* **17**, 779 (2014).