

Project Title: Monocytes as neoangiogenesis promoters and anti-cancer targets

Supervisor: Jacinta Serpa, PhD
CEDOC-NMS, IPOLFG
<http://cedoc.unl.pt/>
<http://www.ipolisboa.min-saude.pt>
Contact: jacinta.serpa@nms.unl.pt; 966177301

Location of research lab/research center:
Instituto Português de Oncologia de Lisboa, EPE

Summary: (1000 characters)

The role of monocytes in endothelial cells (EC) differentiation, contributing for vessels network repair and renewal have been recently shown in inflammation, cardiovascular and hematological diseases. Our *in vitro* preliminary results show that monocytes cultured in special conditions can differentiate into ECs and monocytes from cancer patients have an increased potential of EC differentiation.

It is known that some drugs (β -blockers, HDACs inhibitors and thalidomide and analogs), already approved for human use, have simultaneously a pro-apoptotic role in EC and a modulatory role in monocytes differentiation.

Neoangiogenesis is a crucial step in cancer and the anti-angiogenic strategy has been disappointing so far. Hence, we hypothesized that these drugs can be used to treat cancer by disturbing neoangiogenesis and vessels stability.

This project will disclose the mechanism underlying monocytes differentiation into ECs, the usefulness of monocytes levels as a prognostic factor for cancer progression and the validation of some of these drugs as an alternative to fight cancer.

Bibliographic references:

- 1 Folkman, J. Tumor angiogenesis: therapeutic implications. *The New England journal of medicine* **285**, 1182-1186, doi:10.1056/NEJM197111182852108 (1971).
- 2 Jaipersad, A. S., Lip, G. Y., Silverman, S. & Shantsila, E. The role of monocytes in angiogenesis and atherosclerosis. *Journal of the American College of Cardiology* **63**, 1-11, doi:10.1016/j.jacc.2013.09.019 (2014).
- 7 Wang, X. B., Tian, X. Y., Li, Y., Li, B. & Li, Z. Elevated expression of macrophage migration inhibitory factor correlates with tumor recurrence and poor prognosis of patients with gliomas. *Journal of neuro-oncology* **106**, 43-51, doi:10.1007/s11060-011-0640-3 (2012).
- 8 Liao, X. *et al.* The beta-adrenoceptor antagonist, propranolol, induces human gastric cancer cell apoptosis and cell cycle arrest via inhibiting nuclear factor kappaB signaling. *Oncology reports* **24**, 1669-1676 (2010).
- 11 Morotti, A. *et al.* Valproate enhances imatinib-induced growth arrest and apoptosis in chronic myeloid leukemia cells. *Cancer* **106**, 1188-1196, doi:10.1002/cncr.21725 (2006).
- 16 Gockel, H. R. *et al.* Thalidomide induces apoptosis in human monocytes by using a cytochrome c-dependent pathway. *Journal of immunology* **172**, 5103-5109 (2004).
- 18 Silva, G., Cardoso, B. A., Belo, H. & Almeida, A. M. Vorinostat induces apoptosis and differentiation in myeloid malignancies: genetic and molecular mechanisms. *PLoS one* **8**, e53766, doi:10.1371/journal.pone.0053766 (2013).