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The decrease of MITF, a crucial melanoma transcription factor does not induce marks of epithelial-mesenchymal transition, maintains the proliferation and invasivity, but diminish the differentiation of melanoma cells

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Melanoma is an aggressive cancer of the skin in which microheterogeneity appears early after its onset. Epithelial-mesenchymal transition (EMT) is a key process associated with the progression of malignant tumors. It is believed that low levels of MITF, a melanoma pivotal transcription factor, are associated with EMT-like phenotype. The phenotype switching model in melanoma predicts that low-MITF protein levels favor tumor cell invasivity, but slow down proliferation and inhibit differentiation, while high-MITF cells are highly differentiated and rapidly proliferating. To verify this in the cell culture model, we have developed the Tet-On lentiviral inducible system based on the Tet-pLKO-puro plasmid with cloned shRNA to stepwise decrease MITF level in six melanoma cell lines with high MITF. The MITF levels substantially decreased after the addition of doxycycline. Surprisingly, all cell lines proliferated equally despite the low MITF protein level and did not seem to be more invasive. Proteins characteristic for EMT were either present or lacking without any changes. BCL2 protein did not display any change. The only changes were the decrease of E-cadherin in MeWo cells and increase of N-cadherin in SK-MEL-28 cells, two typical hallmarks of EMT. Genes responsible for pigmentation (TYR, TRP1 and 2), the expression of which requires MITF, were decreased after addition of doxycycline in low-MITF cells, by RT-PCR. Experiments in nude mice xenografts are underway. In sum, the results predict that MITF levels generally may reflect rather than directly cause the EMT in melanoma *in vitro*.

Biography

Jiri Vachtenheim received his MD from the Medical School of the Charles University, Prague in 1981 and PhD degree in 1985. Parts of his Post-doctoral studies were performed as fellowships in Great Britain and Belgium. He is now an Associate Professor and Department Head at the Institute of Medical Biochemistry and Laboratory Diagnostics, First Faculty of Medicine, Charles University, Prague, Czech Republic. He has published more than 40 papers in reputed journals and has served as a reviewer of many publications and grants.

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