THE EFFECT OF AMINO ACID DEPRIVATION ON THE GROWTH SIGNALING IN MALIGNANT MELANOMA

Dorotíková A.[1,2], Vadovičová N.[1,2], Uldrijan S.[1,2]

[1]*Masaryk University, Faculty of Medicine, Brno, Czech Republic*
[2]*International Clinical Research Center, St. Anne's University Hospital Brno, Brno, Czech Republic*

The mTORC1 signaling pathway is a crucial regulator of cancer cell growth, survival, and metabolism. Among its various features, it responds to the level of amino acids via specific sensors. Methionine, an essential amino acid, is sensed indirectly through its metabolite S-adenosylmethionine, which binds to the sensor SAMTOR and enables mTORC1 activation. Its presence in the cell is vital for cell proliferation and growth of many cancer types.
We analyzed the impact of methionine deprivation on mTORC1 activity in *BRAF*-mutated melanoma cells. Based on the current knowledge, we expected mTORC1 inhibition after methionine restriction. Surprisingly, in *BRAF*-mutant cells, we observed an increase in mTORC1 activity. Moreover, this activation correlated with the increased activity of ERK and AMPK signaling pathways, which are closely connected to the mTOR signaling and growth regulation. Altogether our data indicate the involvement of another unknown regulatory loop affecting the mTORC1 signaling in *BRAF*-mutant melanoma cells after methionine restriction.

This work was funded by the Czech Science Foundation (GA22-30397S), the European Regional Development Fund - Project ENOCH (No. CZ.02.1.01/0.0/0.0/16_019/0000868), the European Union – Next Generation EU - the project National Institute for Cancer Research (Programme EXCELES, Project No. LX22NPO5102), and Brno city municipality (Brno Ph.D. Talent Scholarship).