miR-451 expression impacts key biological processes through regulation of PI3K/AKT pathway and sensitizes human head and neck cancer cell lines to Allitinib - a EGFR inhibitor.

Rocha AO[1]*, Lengert AH[1],Oliveira RJ[1], Ferreira FC[1],Silva VA[1], ReisRM[1,2],Carvalho AL[1], VidalDO[1]*.

[1]Molecular Oncology Research Center – Barretos Cancer Hospital, Barretos, Brazil
[2]Life and Health Sciences Research Institute (ICVS), University of Minho, Braga, Portugal.
*For correspondence: rochaalline@hotmail.com; danielovidal@gmail.com.

Introduction: MicroRNAs (miRNAs) are a class of small non-coding RNAs involved in gene expression regulation. They have important roles in several biological processes such as cell development, differentiation, cell cycle regulation, proliferation, migration, invasion, apoptosis and chemoresistance. MicroRNA-451has emerged as an important tumor suppressor that is downregulated in several tumor types. Moreover, activation of the PI3K/AKT signaling pathwayhas been associated with the loss of miR-451 expression and poor prognosis inhead and neck squamous cell (HNSCC). Activation of PI3K/AKT pathway has been described as an important mechanism implicated in tumor progression and resistance to epidermal growth factor receptor (EGFR) inhibitors. Up to 90% HNSCC present higher expression levels of EGFR, this is associated with poor prognosis. Allitinib is a new irreversible and promising selective EGFR inhibitor for the treatment of solid tumors. **Objectives:** We evaluated the biological role of miR-451 overexpression in head and neck cancer cell lines, and its impact in the response to Allitinib treatment in these cell lines. **Methods:** We determined miR-451 expression in six human HNSCC cell lines by RT-qPCR. Overexpression of miR-451 was performed in two cell lines (JHU-12 and JHU-28) and functional assays were conducted to assess its biological impact regarding invasion, migration, proliferation, apoptosis, cytotoxicity and colony formation. We also evaluated the protein levels of PI3K/AKT pathway members by western blotting. The role of miR-451 overexpression in Allatinib treatment was evaluated monitoring the cell viability using MTS assay. **Results:** miR-451 overexpression inhibited migration and clonogenic potential of JHU-12, and invasion capacity of JHU-28. Furthermore, we observed a reduction of proliferation rate in JHU-12 and JHU-28. Also, miR-451 overexpression was associated with lower protein levels of PI3K and phosphorylated AKT. Interestingly, we observed that miR-451 transfected JHU-28 cell line was more sensitive to Allitinib treatment. **Conclusion:** Our results demonstrated that miR-451 should be involved in the control of progression and metastatic potential in HNSCC, potentially through the regulation of PI3K/AKT pathway. Also, our data demonstrated that miR-451 overexpression might sensitize HNSCC cell line to Allitinib treatment, and its role as a potential new strategy for the treatment of chemo resistant HNSCC need to be explored.

Financial support: FAPESP (nº. 2012/23326-6) and Barretos Cancer Hospital.

Abstract Submission and Guidelines

Abstract Guidelines
Please submit a short abstract no longer than 500 words (or 3.500 characters) of your proposed presentation in a specific session.

Font, Margins, Layout
• Arial 10-point font
• 1-inch margins (top, bottom, left, right)
• Left-justify all text
• Single-space all text except as indicated below

Organization
• Abstract should consist of the following elements:

1. Title, in boldface font - sentence case; 1 blank line
2. Author information (including institutions and countries), please underline the name of the presenting author; 1 blank line
3. Body of abstract in a single paragraph, limited to only 500 words.

Size, file type
• Abstract body limited to 500 words

Important:

• File must be submitted as a Word document (.doc / .docx).
• A sample abstractis provided for reference at the website.