

Propositions belonging to the thesis of Fabrizio Picchione:

## **Screening for Novel Genes Contributing to the Transformed Status of Alveolar Rhabdomyosarcoma (ARMS)**

- 1- PAX3-FOXO1 alone is not sufficient to induce cellular transformation.

This thesis

Lagutina et al. (2002) Mol Cel Biol; 22, 7204-7216

Keller et al. (2004) Genes Dev; 18 2614-2626

- 2- The use of a RH30 cell line ARMS cDNA library screen is a useful method to identify PAX3-FOXO1 cooperating genes never associated with cancer formation.

This thesis

- 3- IRIZIO encodes multiple splice variants, but only one efficiently cooperates with PAX3-FOXO1 in the transformation of primary Arf<sup>-/-</sup> myoblasts.

This thesis

- 4- Although often present in human malignancies, p53 mutations are quite rare in ARMS.

This thesis

- 5- Up-regulation of Plod family members (lysyl hydroxylase 1-3) is associated with human cancer.

This thesis

- 6- The use an Affimetrix array analysis of primary mouse myoblasts expressing PAX3-FOXO1 may represent an unbiased model to identify genes directly controlled by the fusion protein.

This thesis

- 7- Although Ni Chonghaile et al. identified that mitochondrial priming in *in vitro* culture correlates with clinical response and long-term patient survival, in various AML, ALL and ovarian cancer, their results do not imply that the approach will be generally efficacious in solid tumors.

Ni Chonghaile et al., (2011). Science;334(6059):1129-33

- 8- The work of Soria et al. shows that transcription of p53 target genes can be inactivated by a novel mechanism of epigenetic chromatin remodeling after adenoviral infection, opening new strategies for oncolytic viral therapy. However this work does not discuss a possible therapeutic advantage of oncolytic adenovirus infection of tumors without p53 abnormalities.

Soria et al. (2010). Nature; 466(7310): 1076–1081

- 9- The conclusion of Agrawal et al. that identification of inactivating mutations in *NOTCH1* in 40% of head and neck squamous cell carcinomas suggests that *NOTCH1* functions as a tumor suppressor in this disease is preliminary without functional verification in animal models.

Agrawal et al. (2011). Science; 333(6046):1154-7

- 10- Without knowing the hybridization efficiency of micro RNAs to ceRNAs Tay et al fail to explain in their paper describing gene regulation via ceRNAs why knockdown of PTEN RNA has such a dramatic effect on genes, whose expression is so much higher than that of PTEN.

Tay et al. (2011). Cell 147, Issue 2, 344-357

- 11- Although it has been demonstrated that full-term mice can be generated from iPSCs using the tetraploid complementation method, a postnatal evaluation of the iPSC-derived mice has not been determined.

Zhao et al. (2009) Nature; 461(7260):86-90

Boland et al. (2009) Nature; 461(7260):91-4

- 12- The phrase “Success in life has nothing to do with what you gain in life or accomplish for yourself. It's what you do for others” represents SJCRH mission.

Danny Thomas