

Unexpected antagonistic roles of Vav family proteins as tumor promoters and suppressors

Xosé R. Bustelo

Profesor de Investigación del CSIC en el Centro de Investigación del Cáncer (CIC)-Salamanca

Vice-director del Centro de Investigación del Cáncer (CIC)-Salamanca

Coordinador del Programa de Mecanismos de Progresión Tumoral CIBERONC del Instituto de Salud Carlos III

Presidente de ASEICA

Rho GDP / GTP
exchange factors

(GEFs) are enzymes that promote the activation of Rho GTPases in both normal and cancer cells. Our group is trying to address these issues using as main tool the three known members of the Vav GEF family, the proteins Vav1, Vav2 and Vav3. We demonstrated that the endogenous wild type and mutant versions of these proteins play proactive roles in mature T cell leukemia and a variety of epithelial tumors. Also, our "pharmaco-mimetic" knock-in mice demonstrating that the inhibition of GEFs does have a negative impact on the fitness of tumor cells in vivo.

These studies also have revealed the ugliness of dissociating the positive and negative effects elicited by the inhibition of Vav proteins depending on the level of catalytic silencing achieved at the organismal level. Furthermore, a member of this family, Vav1, can unexpectedly play catalysis-independent tumor suppression roles in immature, TLX + T-cell acute lymphoblastic leukemia. The elimination of this function seems to be critical for the pathogenesis of this leukemia subtype.

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**Moderador: Luis Verde,
Gerente XXIAC**

Organiza: Grupo CellCOM. INIBIC
Contacto: ma.Dolores.Mayan.Santos@sergas.es



SERVIZO
GALEGO
de SAÚDE

Área Sanitaria da Coruña e Cee



instituto de
investigación biomédica
de la coruña



FUNDACIÓN PROFESOR
NOVOA SANTOS