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THE ANTITUMOR DRUG VINBLASTINE INDUCES THE PHOSPHORYLATION OF ANNEXIN A2

**Fernandez-Garcia B¹, Casado P¹, Prado MA¹, Ugarte LJ¹, Calvo E²,
López JA², Ramos S¹ and Lazo PS¹**

¹Departamento de Bioquímica y Biología Molecular, Instituto Universitario de Oncología del Principado de Asturias (IUOPA), Universidad de Oviedo, 33071, Oviedo, Spain

²Unidad de Proteómica, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain.

Vinblastine (Vb) is an antitumor drug that inhibits microtubule polymerization, causes G2/M arrest and induces cell death. 2D-PAGE and MALDI-ToF-MS analysis on A549 cells, revealed that vinblastine upregulates an acidic form of the protein Annexin A2. The staining of this Vb induced form of Annexin A2 with the phosphospecific dye Pro-Q Diamond, indicates the presence of phosphorylated Annexin A2 in this spot. Moreover, this Vb up-regulated form of Annexin A2 disappears upon treatment with λ -protein phosphatase, confirming this post-translational modification. Further analysis using MRM (multiple reaction monitoring) indicated the presence of a phosphorylated peptide, containing threonine 19, serine 18 or serine 22, only in the vincristine upregulated form. MS/MS spectra show a clear phosphorylation of Thr19 and lower signals for Ser18 and Ser22. These results indicate that phosphorylation of Annexin A2 in different residues may play a role in the cellular response to Vinblastine.