BMC Pharmacology

Meeting abstract

PI3Kδ: a double-edged sword in leukemia formation

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from 13th Scientific Symposium of the Austrian Pharmacological Society (APHAR). Joint Meeting with the Austrian Society of Toxicology (ASTOX) and the Hungarian Society for Experimental and Clinical Pharmacology (MFT)
Vienna, Austria. 22–24 November 2007

Published: 14 November 2007

BMC Pharmacology 2007, **7**(Suppl 2):A7 doi:10.1186/1471-2210-7-S2-A7

This abstract is available from: http://www.biomedcentral.com/1471-2210/7/S2/A7

The PI3Kδ isoform is a candidate drug target in leukemia. Here, we explored its role in Abelson-induced leukemia. Frank leukemia emerges if the tumor cells have managed to outwit the immune system. The absence of PI3Kδ affected both the tumor cells and the NK cells. Abelson-transformed PI3Kδ$^{-/-}$ cells induced leukemia in RAG2$^{-/-}$ animals with a significantly increased latency, implicating PI3Kδ in tumor progression. NK cell function, however, was also contingent on PI3Kδ. PI3Kδ$^{-/-}$ NK cells failed to lyse target cells. Capacitance measurements revealed the underlying defect: in PI3Kδ$^{-/-}$ NK cells lytic granules did not fuse with the cell membrane. Accordingly, transplanted leukemic cells killed PI3Kδ$^{-/-}$ animals more rapidly, both in syngeneic (PI3Kδ$^{-/-}$) or immunocompromised (RAG2$^{-/-}$ PI3Kδ$^{-/-}$) animals. Our observations define a dual function of PI3Kδ in leukemia and document that the action of PI3Kδ in the NK compartment is as relevant to the survival of the mice as the delayed tumor progression.