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The Eya Phosphatase: its unique role in cancer

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Abstract

The Eya proteins were originally identified as essential transcriptional co-activators of the Six family of homeoproteins. Subsequently, the highly conserved C-terminal domains of the Eya proteins were discovered to act as a Mg^{2+} -dependent Tyr phosphatases, making Eyas the first transcriptional activators to harbor intrinsic phosphatase activity. Only two direct targets of the Eya Tyr phosphatase have been identified: H2AX, whose dephosphorylation directs cells to the DNA repair instead of the apoptotic pathway upon DNA damage, and ER β , whose dephosphorylation inhibits its anti-tumor transcriptional activity. The Eya Tyr phosphatase mediates breast cancer cell transformation, migration, invasion, as well as metastasis, through targets not yet identified. Intriguingly, the N-terminal domain of Eya contains a separate Ser/Thr phosphatase activity implicated in innate immunity and in regulating c-Myc stability. Thus, Eya proteins are highly complex, containing two separable phosphatase domains and a transcriptional activation domain, thereby influencing tumor progression through multiple mechanisms.

Keywords: Phosphatase; Cancer; Eya; Inhibitor; Biochemistry

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