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The Eya Phosphatase: its unique role in cancer

Hengbo Zhou [1,2,†], Lingdi Zhang [3,†], Rebecca L. Vartuli [1,4], Heide L. Ford [1], Rui Zhao [3,*]

1. Department of Pharmacology, University of Colorado Denver Anschutz Medical Campus
2. Cancer Biology Program
3. Department of Biochemistry and Molecular Genetics, University of Colorado Denver Anschutz Medical Campus
4. Molecular Biology Program

† These authors contributed equally to this work.
* Corresponding author. rui.zhao@ucdenver.edu

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 ERβ, 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