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Title: ***An unregulated regulator: Vasa expression in the development of somatic cells and in tumorigenesis***

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Summary

Growing evidence in diverse organisms shows that genes originally thought to function uniquely in the germ line may also function in somatic cells, and in some cases even contribute to tumorigenesis. Here we review the somatic functions of Vasa, one of the most conserved "germ line" factors among metazoans. Vasa expression in somatic cells is tightly regulated and often transient during normal development, and appears to play essential roles in regulation of embryonic cells and regenerative tissues. Its dysregulation, however, is believed to be an important element of tumorigenic cell regulation. In this perspectives paper, we propose how some conserved functions of Vasa may be selected for somatic cell regulation, including its potential impact on efficient and localized translational activities and in some cases on cellular malfunctioning and tumorigenesis.

Keywords: Vasa; DDX4; germ line factors; tumorigenesis; translation

Introduction

More than 40 genes that are normally expressed selectively in the germ line of many model organisms are also expressed in various tumor types in humans (Simpson et al., 2005). Recapitulating functions of a germ line program thus has been hypothesized to contribute to the characteristic features of neoplastic diseases, including immortality, hypomethylation of DNA, and metastatic migrations (Hanahan and Weinberg, 2011). Indeed, in *C. elegans*, mutations of the retinoblastoma (Rb) tumor suppressor complex induce somatic cells to express germ line genes, leading cells to revert to patterns of gene expression normally restricted to germ cells (Wang et al., 2005). Further, *C. elegans* mutants with decreased insulin-like signaling (e.g. *daf-2*, the insulin-like receptor, and *age-1*, the downstream PI3K mutant strains) cause mis-expression of the germ line factors *pie-1* and *pgl* in the somatic cells. These altered somatic cells are then more resistant to stress-induced damage and have increased cellular lifespans (or negligible senescence) (Curran et al., 2009). This result is particularly noteworthy considering *C. elegans* somatic cells are genetically programmed to cease cell divisions after the animal reaches adulthood. These observations suggest that the acquisition of germ line elements may contribute to somatic phenotypes, and even of tumorgenic cells.

Vasa was first identified in *Drosophila* (Hay et al., 1988; Lasko and Ashuburner, 1988) as a polar