Editorial

The Nucleophosmin-Pin1 interaction links the cell cycle, cancer and pluripotency

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In the current issue of J Mol Biochem, Zhao *et al.* (2015) characterize the phosphorylation sites of nucleophosmin (Npm); a protein involved, among others, in licensing of centrosome duplication during the cell cycle. The authors also identify a functional interaction of Npm with the Pin1 isomerase, taking place during mitosis. They show that mutating one of the possible Npm binding sites results in cell division defects and a decrease in mitotic cell number. The latter is of special significance, suggesting that Npm post-phosphorylation plays a role in cell cycle progression. But perhaps the most interesting aspect in this story is the emerging link between the cell cycle, cancer and pluripotency.

Excessive centrosome numbers have been reported to disrupt proper chromosome segregation, which, in turn, is correlated to oncogenesis (Godinho & Pellman 2014). In line with this, high *Pin1* expression has been reported in a plethora of human cancers (Bao *et al.* 2004), and has been associated with poor prognosis (reviewed by Lu & Hunter 2014). Its overexpression has been reported to induce chromosomal instability, *in vitro* cell transformation as well as malignant mammary tumors in transgenic mice (Suizu *et al.* 2006). In addition, *Npm* is overexpressed in a large number of human cancers (reviewed by Grisendi *et al.* 2006) and has been proposed to have oncogenic properties (Lim & Wang 2006) but its ablation has also been linked to centrosome overduplication and genomic instability (Grisendi *et al.* 2005).

Interestingly, both NPM and Pin1 are linked to pluripotency. The former was first identified in a genome-wide screen for pluripotency regulators; further analysis suggested that it promotes the self-renewal of embryonic stem (ES) cells via the RNA-binding protein Mki67ip (Abujarour *et al.* 2010). In line with this, Johansson and Simonsson (2010) found that, in ES cells, each of the core ES cell transcription factors Oct4, Sox2 and Nanog independently formed complexes with Npm1. They further showed that these interactions were affected by the routes of differentiation and that *Npm1* downregulation increased the expression of mesodermal and ectodermal genes, while they identified that Npm also interacts with Translationally controlled tumor protein (Tpt1) during ES cell mitosis (Johansson *et al.* 2010). Similarly, Pin1 was found to interact and stabilise Nanog, a critical mechanism for their ability to self-renew and form teratomas in mice (Moretto-Zita *et al.* 2010). Nishi *et al.* (2011) showed that Pin1 also regulates phosphorylated Oct4 and is essential for the maintenance of the pluripotent state.

All the above can be seen within a new context, with the novel identification of Npm-Pin1 interaction, reported in this issue. The interplay between the cell cycle, pluripotency and cancer has only recently gained attention and seems to be extremely complicated and multidirectional (Champeris Tsaniras *et al.* 2014); however, a better understanding is on the way, as more and more links begin to unravel.

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