The p-bodies and reinitiate translation (11). p-bodies increase

Theinositol phosphate family is an important family of signalling molecules thatwas discovered in the 1920s and is conserved from yeast to humans. All themembers of this family are derived from myo-inositol and are involved incytoplasmic and nuclear signalling.

The hydroxyl groups of the inositol ringcan be phosphorylated in a combinatorial manner. Inositol hexakisphosphate (IP6)is the most abundant inositol phosphate and is generated from IP5 byinositol pentakisphosphate 2 kinase (IPPK) (1). In mammals, IP6 further gives rise to high energypyrophosphate molecules (2), IP7 and IP8, by the actionof IP6 kinases (IP6K1, IP6K2 and IP6K3) and IP7 kinases(PPIP5K1 and PPIP5K2). IP6K1 is implicated in a number of cellular processes inmice such as vesicular trafficking (3), insulin secretion (4, 5), male fertility(5), neutrophil phagocytosis (6), blood clotting (7) and DNA repair (8, 9).

IP6K1modulates protein functions by mainly three mechanisms: a) IP7 synthesizedby IP6K1 can pyrophosphorylate proteins, b) IP7 can directly bind toproteins, and c) IP6K1, independent of its catalytic activity, can alsodirectly bind to proteins and modulate their functions. Processingbodies (P-bodies) are small membrane-less cytoplasmic foci that are involved inmRNA degradation (10) and storage (11). mRNA in the cytoplasm is targeted todegradation by either exosome mediated 3′-5′ degradation or 5′-3’exoribonuclease mediated degradation (12). mRNA deadenylation precedes boththese decay pathways (13). All the enzymes involved in 5′-3′ degradationpathway are localized to P-bodies (14-19). However, not all mRNA that islocalized to P-bodies is targeted for degradation as they can also escape P-bodiesand reinitiate translation (11). P-bodies increase in size

when mRNA decay isinhibited and reduce in size and number if mRNA deadenylation is blocked or ifone of the scaffolding proteins is missing (10). P-bodies are involved in mRNA surveillance (20), gene silencing (21), degradation of mRNA containing AU rich elements (22) andtranslational repression.

P-bodies are dynamic and motile entities that formwhen the abundance of stalled mRNA increases in the cytoplasm (23). Thisimplies that the size and number of P-bodies depend on the amount of mRNAundergoing de-capping. To enter P-bodies mRNA has to be released frompolysomes. Translation inhibiting drugs like cycloheximide that block mRNA onpolysomes reduce the number of P-bodies drastically whereas drugs likepuromycin that block translation by releasing the mRNA from polysomes inducemore P-bodies (10).

Theproteins present in P-bodies are generally also diffused in the cytoplasm andthere is dynamic flow of proteins in and out of P-bodies. Hence, changes in P-body number and size percell is related to the cell cycle phase, proliferation status of the cell andavailability of nutrients (24). Ip6k1-/-male mice are infertile (5). Our lab has shown that IP6K1 protein isindispensable for the differentiation of round spermatids and is required forregulating the assembly of chromatoid bodies during spermiogenesis (Malla etal., unpublished).

A chromatoid body is a dense structure in the cytoplasmof male germ cells and is mainly composed of RNA and RNA binding proteins andis thus a type of RNP granule, similar to P-bodies. It was observed that thesechromatoid

bodies are depleted in male germ cells of Ip6k1-/- knockout mice and Ip6k1-/- mouse embryonic fibroblasts (MEFs) havediminished P-bodies compared to Ip6k1+/+MEFs.