New potential role of Vps34 kinase in the control of the cell size

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Platelets, the smallest blood cells, are produced in the bone marrow by their precursors, megakaryocytes (MKs). One of the most characteristic features of the MK maturation is a substantial increase in size, together with the polyploidization of the nucleus. At the end of the maturation process, MKs generate prolonged cytoplasmic protrusions, termed proplatelets, which extend through the vascular sinusoids of the bone marrow and release platelets into the bloodstream. Phosphoinositides are small membrane phospholipids implicated in cellular signalling, organelle trafficking and cytoskeletal dynamics. Phosphatidylinositol 3-monophosphate (PI3P), which is mainly produced by the Vps34 kinase, is a key component in vesicular trafficking processes, as well as autophagy and mTOR signaling. Nucleolus is nuclear subcompartment rich in RNA and RNA-protein complexes. It is the site of different steps of ribosome biogenesis, including transcription of ribosomal genes (rDNAs) and processing of ribosomal RNAs (rRNAs). In this study we show that in immature small MKs majority of Vps34 kinase localizes in organized structures within nucleolus, in fibrillar center (FC), where transcription of rDNA occurs. Treatment of MKs with RNA Pol I inhibitors abolishes Vps34 localization in nucleolus. In addition, when we specifically inhibit Vps34 in immature MKs, they fail to increase in size, and express lower levels of GPIb, indicating failure in maturation. All together, these data indicate that Vps34 might play an important, still undescribed, role in the nucleolar structure organization and/or in the control of MKs size and maturation via ribosome biogenesis. Additional studies are underway for better understanding of these events.

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