
The Bioethics Unit and the Research Ethics Committee (REC) of the Istituto Superiore di Sanità (ISS: Italian National Institute of Health), in charge of dealing with research integrity matters, carried out an independent investigation following the Expression of Concern\(^1\) published by the Journal.

The corresponding author, Dr. Raffaella Guerriero, provided relevant and pertinent documentation and information related to the expression of concern\(^1\), including a chronology of events that is consistent with the one given by the executive editor, Dr. Sharon Ahmad.

In summary, the Guerriero et al. study\(^2\) shows that the mTOR pathway has a prevalent role in the megakaryocitopoiesis by regulating proliferation, maturation, poliploidy and cell size\(^2\).

As already notified, original data related to Figure 5, object of concern, are no longer available.

The authors assert that western blotting results of phosphorylated kinases shown in figure 5 were obtained from samples loaded within gel and equal loading was checked by probing again the membranes with antibodies recognising total proteins.

The panel of figure 5 includes six lanes with thrombopoietin (TPO) in combination or not with four kinase inhibitors and the paper does not discuss all results relative to the figure; some data were already known or additional, but not meaningful for the findings of the work.

Conclusions are based on several data-based findings and on a review of the literature in this topic at the time of preparation of the manuscript. Moreover two independent following papers describe and confirm part of the conclusions reported by the authors \(^3,4\).

Raslova et al (2006)\(^3\) showed that rapamicin, a mTOR inhibitor, causes the inhibition of megakaryocytes poliploidization in cultures of human megakaryocytes, as observed by Guerriero et al\(^2\).

Liu et al. (2011)\(^4\) have evidences that mTOR is responsible for differences during the development of human megakaryocytes. Neonatal megakaryocytes are hyper-proliferative with a lower ploidy during the maturation in comparison with the adult ones. These developmental differences are
associated with up-regulated thrombopoietin signalling through mammalian target of rapamycin (mTOR) and elevated levels of full-length GATA-1 and its target.

In conclusion, the ISS Bioethics Unit and the ISS REC reviewed and confirmed results and conclusions of the paper by Guerriero et al. (2006).

The Head of the ISS Research Coordination and Support Service was informed about the results of such investigation.

The President of the ISS, Prof. Silvio Brusaferro, approved the results of the investigation and the present document.

(Carlo Petrini)
Director of the Bioethics Unit
Chair of the Research Ethics Committee

References


