Check for updates



not clear whether this is significant in an activated platelet. The evidence that panPKC inhibitors abolish phosphorylation of syntaxin as well as secretion is indicative that syntaxin phosphorylation could be important for secretion.[5]

In conclusion, we emphasize that our data[2] are supported by a recent independent study[4] that confirms a positive regulatory role for PKCθ in platelets.

**Satya P. Kunapuli**
*Department of Physiology*
*Temple University Medical School*
*Philadelphia, PA*

**Jianguo Jin**
*Department of Physiology*
*Temple University Medical School*
*Philadelphia, PA*

**Acknowledgments:** We thank Ms Monica Dupon for her help in breeding and genotyping the knockout mice.

This work was supported by research grants HL60683 and HL93231 from the National Institutes of Health.

Approval was obtained from Temple University institutional review board for the studies. Informed consent was provided in accordance with the declaration of Helsinki.

**Contribution:** S.P.K. wrote the response and provided overall supervision and interpretation of the data; and J.J. performed the experiments.

**Conflict-of-interest disclosure:** The authors declare no competing financial interests.

**Correspondence:** Satya P. Kunapuli, PhD, Department of Physiology, Temple University Medical School, Philadelphia PA 19140; e-mail: satya.kunapuli@temple.edu.

## References

1. Harper MT, Poole AW. PKCtheta in platelet activaiton. *Blood.* 2009;114:0.
2. Nagy B Jr, Bhavaraju K, Getz T, Bynagari YS, Kim S, Kunapuli SP. Impaired activation of platelets lacking protein kinase C-theta isoform. *Blood.* 2009;113: 2557-2567.
3. Hall KJ, Harper MT, Gilio K, Cosemans JM, Heemskerk JW, Poole AW. Genetic analysis of the role of protein kinase Ctheta in platelet function and thrombus formation. *PLoS ONE.* 2008;3:e3277.
4. Cohen S, Braiman A, Shubinsky G, Ohayon A, Altman A, Isakov N. PKCtheta is required for hemostasis and positive regulation of thrombin-induced platelet aggregation and alpha-granule secretion. *Biochem Biophys Res Commun.* 2009.
5. Chung SH, Polgar J, Reed GL. Protein kinase C phosphorylation of syntaxin 4 in thrombin-activated human platelets. *J Biol Chem.* 2000;275:25286-25291.
6. Flaumenhaft R, Croce K, Chen E, Furie B, Furie BC. Proteins of the exocytotic core complex mediate platelet alpha-granule secretion. Roles of vesicle-associated membrane protein, SNAP-23, and syntaxin 4. *J Biol Chem.* 1999; 274:2492-2501.

# To the editor:

## β1-tubulin gene mutation platelets are not macrothrombocytes

The brief report by Kunishima et al[1] describing a mutation of the β1 tubulin gene affecting microtubule assembly is of interest, but data presented do not support association of the genetic defect with macrothrombocytopenia. The authors stated both the male propositus and his mother had prominent appearance of giant platelets on peripheral blood smears, and provided light (Figure 1A[1]) and electron micrographs (Figure 1B[1]) to support that finding. The patient platelet in Figure 1A[1] has damaged peripheral cytoplasm that may make it appear larger than a normal cell, but, more important, the platelet is significantly smaller than any red blood cell in the same field. No discoid platelets from the control or patient are present in the electron micrographs (Figure 1B[1]). As a result, it is difficult to be certain there is any real size difference between patient and control platelets. Surely the authors must be aware that giant platelets from all of the known macrothrombocytopenias are larger than red blood cells, and many exceed the size of lymphocytes, monocytes, and neutrophils.[2] It might have been helpful if the authors had provided the mean platelet volumes of the mother and child.

The immunofluorescence studies raise 2 questions. Patient and control microtubule coils in the report's Figure 2A[1] are similar in size and appear to be perfect coils. If the patients had complete platelet microtubule coils, those coils should be many times the diameter of control coils. More important, giant platelets from the known inherited macrothrombocytopenias rarely have complete microtubule coils lying just under the surface membrane. Rather, the giant platelets are spherical in form, and their microtubules are often organized in a manner resembling balls of yarn.[3] The studies of the mutation in the present study are of interest. However, the statement "W318 β1 tubulin may interfere with normal platelet production, resulting in macrothrombocytopenia"[1] is not supported by the data presented.

**James G. White**
*University of Minnesota School of Medicine*
*Minneapolis, MN*

**Conflict-of-interest disclosure:** The author declares no competing financial interests.

**Correspondence:** James G. White, MD, Regents' Professor, Laboratory Medicine, Pathology, and Pediatrics, University of Minnesota School of Medicine, Mayo Bdg, Box MMC 490, 420 Delaware St SE, Minneapolis, MN 55455; e-mail: white003@umn.edu.

## References

1. Kunishima S, Kobayashi R, Itoh TJ, Hamaguchi M, Saito H. Mutation of the beta1-tubulin gene associated with congenital macrothrombocytopenia affecting microtubule assembly. *Blood.* 2009;113:458-461.
2. White JG. Structural defects in inherited and giant platelet disorders. *Adv Hum Genet.* 1990;19:133-234.
3. White JG, Sauk JJ. The organization of microtubules and microtubule coils in giant platelet disorders. *Am J Pathol.* 1984;116:514-522.

# Response

## W318 β1-tubulin and macrothrombocytopenia

We would like to thank Dr White for valuable comments on our study that reported the first human β1-tubulin mutation associated with congenital macrothrombocytopenia.[1] We have been working on congenital macrothrombocytopenia and analyzed more than 200 cases. We do not think that giant platelets from macrothrombocytopenia syndromes are necessarily larger than red blood cells. The mean platelet sizes

Downloaded from http://ashpublications.org/blood/article-pdf/114/2/492/1319575/zh802809000492.pdf by guest on 02 November 2024