Could TCTP contribute to Armin Braun's paradigm of tumor reversion in plants?

Robert Amson, Jacek Kubiak, Marc Van Montagu, Adam Telerman

Cell Cycle 10:1, 1-1; January 1, 2011; © 2011 Landes Bioscience

Could TCTP contribute to Armin Braun's paradigm of tumor reversion in plants?

Robert Amson,[1] Jacek Z. Kubiak,[2] Marc Van Montagu[3] and Adam Telerman[1,*]

[1]Laboratoire de biologie et pharmacologie (LBPA); UMR 8113; Ecole Normale Supérieure; Cachan, France; [2]CNRS UMR 6061; Institute of Genetics and Development; Cell Cycle Group; IFR 140 GFAS; Faculty of Medicine; University of Rennes I; Rennes, France; [3]Institute of Plant Biotechnology for Developing Countries (IPBO); Department of Molecular Genetics; Ghent University; Ghent, Belgium

Armin Braun, a plant geneticist in the 1950–60's at the Rockefeller, was the first to provide experimental evidence for tumor reversion in plants.[1] Through setting up his experiments in plants, Braun made of tumor reversion a philogenetically conserved system. With today's understanding of the tumor cell plasticity, pluripotentiality and stemness, Braun's words[1] spelt 50 years ago sound almost magic: "*results of this study indicate that the capacity of teratoma tissue of single cell origin to organize is a reflection of the inherent potentialities of pluripotent tumor cells... clones of teratoma tissue of single-cell origin developed organized structures … a controlled recovery of crown-gall tumor cells could be accomplished*". However, Braun's findings have never been explained at the molecular level, and even their malignant phenotype remains to be explored. By studying tumor reversion in human cancer cells, we found that Translationally Controlled Tumor Protein (TCTP) is a key gene that needs to be switched off in order to quit the malignant process and revert.[2,3] Could TCTP be the molecular link to Armin Braun's findings?

Translationally Controlled Tumor Protein (TCTP) knockout in mice causes embryonic lethality, showing that this gene is essential for development.[4] Most interestingly, Brioudes et al.[5] recently reported that TCTP knockout in plants also resulted in a lethal phenotype. TCTP-lacking adult plants could be rescued by "feeding" the embryos, and the same phenotype, i.e., small size plants, were observed using the RNAi approach. Importantly the KO phenotype of *Arabidopsis thaliana* was rescued by Drosophila TCTP and vice versa. Thus TCTP seems to integrate signals controlling cell cycle progression, proliferation and cell sizing. Brioudes et al. provide considerable insight into these issues through analysis of the first TCTP-lacking adult multicellular organisms. Moreover, this study may provide a missing link with early studies by Armin Braun.

Knocking down Arabidopsis TCTP slows down the cell cycle; G_1-phase, when cells grow, is significantly prolonged (4 hrs) and M-phase entry is reduced. Does TCTP integrate cell sizing into the cell cycle machinery? If yes, it acts both on the S- and M-phase via downregulation of specific markers: PCNA for S- and cyclin B for M-phase. In animal cells TCTP also associates with F-actin fibers at the cell periphery, regulating cell shape both in interphase and in mitosis and cell motility.[6] This interaction may likely be assured through the TCTP cofilin-like domain.[7] On the other hand, the localization of TCTP to the mitotic spindle does not seem to implicate a direct association with microtubules.[6] Hence, TCTP-cytoskeleton interaction becomes elusive and clearly requires more detailed analysis.

Genetic experiments in Drosophila linked TCTP to the TOR pathway.[8] Our data futher indicate that TCTP associates with the protein synthesis-initiation and -elongation machinery.[3] We found that besides interacting with eEF1A, it may also interact with the eIF3 complex (unpublished results), which is under the control of mTOR, as shown by John Blenis' work,[9] providing hereby a potential alternative molecular explanation for the genetic TCTP-TOR connection. TCTP also regulates the expression of *oct4* and *nanog*, early embryonic genes, in nuclear reprogramming, as shown by John Gurdon's group.[10] Thus, TCTP seems more than ever to act on multiple pathways, making simultaneously numerous imprints on cell physiology. This may predispose TCTP to be an omnipresent factor able not only to drive, but also to assist efficiently major cell functions.

With the clear understanding that plant tumors are very different from human ones, nevertheless, to explore to what extend some pathways are conserved, an "easy experiment" would be to test whether silencing of TCTP could revert tumor formation in plants. Conversely, could forced expression of plant TCTP transform our revertants back into aggressive tumor cells? We would have at least some molecular explanations for Braun's results.

Acknowledgments

A.T. and R.A. are supported by the European Union (Conticanet) and ANR- 09-BLAN-0292-01

References

1. Braun AC, et al. Proc Natl Acad Sci USA 1959; 45:932-8.
2. Tuynder M, et al. Proc Natl Acad Sci USA 2002; 99:14976-81.
3. Telerman A, et al. Nat Rev Cancer 2009; 3:206-16.
4. Susini L, et al. Cell Death Differ 2008; 15:1211-20.
5. Brioudes F, et al. Proc Natl Acad Sci USA 2010; 107:16384-9.
6. Bazile F, et al. Carcinogenesis 2009; 30:555-65.
7. Tsarova K, et al. FEBS Lett 2010; 584:4756-60.
8. Hsu YC, et al. Nature 2007; 445:785-8.
9. Ma XM, et al. Nat Rev Mol Cell Biol 2009; 10:307-18.
10. Koziol MJ, et al. Curr Biol 2007; 17:801-7.

*Correspondence to: Adam Telerman; Email: adam.telerman@lbpa.ens-cachan.fr or telerman@noos.fr
Submitted: 11/23/10; Accepted: 11/24/10
Previously published online: www.landesbioscience.com/journals/cc/article/14288
DOI: 10.4161/cc.10.1.14288
Comment on: Brioudes F, et al. Proc Natl Acad Sci USA 2010; 107:16384–9.