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## Editorial Enquiries

*Trends in Cell Biology*

Cell Press

600 Technology Square

Cambridge, MA 02139, USA

Tel: +1 617 386 2105

Fax: +1 617 397 2810

E-mail: tcb@cell.com

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**Cover:** Cell biological research is becoming increasingly three dimensional, taking into account spatial dynamics when studying biological questions. In this special issue of *Trends in Cell Biology*, researchers from across various fields discuss how the inner architecture of the cell, and the external environment that surrounds it, impacts upon cell function. The cover image, Z-stack projections of a mouse mammary organoid grown in Matrigel 3D cultures, provides a striking example of how considering three-dimensional structure can offer insight into behaviour. Cover image courtesy of Ian Macara.