



**Cover:** 3D rendering of the ultrastructure of growth-arrested non-malignant human breast epithelial (HMT-3522-S1) cells within an acinus-like structure, obtained by focused ion beam scanning electron microscopy (FIB-SEM). Cytoskeletal cables (yellow) were found to be enveloped by nuclear membrane tunnels (blue) and connect to the nuclear lamina. See article by D. M. Jorgens et al. (pp. 177–189).

### EDITORIAL

- 1 3D cell biology – the expanding frontier  
**Ewald, A. J. (Editor)**

### FOREWORD

- 3 Goodbye flat biology – time for the 3rd and the 4th dimensions  
**Bissell, M. J.**

### CELL SCIENTISTS TO WATCH

- 7 Interview with the Guest Editor – Andrew Ewald  
11 Cell scientist to watch – Madeline Lancaster

### CELL SCIENCE AT A GLANCE

- 15 Embryo–epithelium interactions during implantation at a glance  
**Aplin, J. D. and Ruane, P. T.**

### COMMENTARIES

- 23 Seeing is believing – multi-scale spatio-temporal imaging towards *in vivo* cell biology  
**Follain, G., Mercier, L., Osmani, N., Harlepp, S. and Goetz, J. G.**
- 39 Microtubules in 3D cell motility  
**Bouchet, B. P. and Akhmanova, A.**
- 51 How cells respond to environmental cues – insights from bio-functionalized substrates  
**Ruprecht, V., Monzo, P., Ravasio, A., Yue, Z., Makhija, E., Strale, P. O., Gauthier, N., Shivashankar, G. V., Studer, V., Albiges-Rizo, C. and Viasnoff, V.**
- 63 3D culture models of tissues under tension  
**Eyckmans, J. and Chen, C. S.**
- 71 Tissue mechanics regulate brain development, homeostasis and disease  
**Barnes, J. M., Przybyla, L. and Weaver, V. M.**

### SHORT REPORTS

- 83 3D electron tomography of brain tissue unveils distinct Golgi structures that sequester cytoplasmic contents in neurons  
**Fernandez-Fernandez, M. R., Ruiz-Garcia, D., Martin-Solana, E., Chichon, F. J., Carrascosa, J. L. and Fernandez, J.-J.**
- 90 Epidermal growth factor suppresses intestinal epithelial cell shedding through a MAPK-dependent pathway  
**Miguel, J. C., Maxwell, A. A., Hsieh, J. J., Harnisch, L. C., Al Alam, D., Polk, D. B., Lien, C.-L., Watson, A. J. M. and Frey, M. R.**

- 97 Myosin II governs collective cell migration behaviour downstream of guidance receptor signalling  
**Combedazou, A., Choessel-Cadamuro, V., Gay, G., Liu, J., Dupré, L., Ramel, D. and Wang, X.**
- 104 A basal cell defect promotes budding of prostatic intraepithelial neoplasia  
**Wang, M., Nagle, R. B., Knudsen, B. S., Rogers, G. C. and Cress, A. E.**
- 111 EphA2 proteomics in human keratinocytes reveals a novel association with afadin and epidermal tight junctions  
**Perez White, B. E., Ventrella, R., Kaplan, N., Cable, C. J., Thomas, P. M. and Getsios, S.**

### RESEARCH ARTICLES

- 119 Cell-cycle-dependent TGF $\beta$ –BMP antagonism regulates neural tube closure by modulating tight junctions  
**Amarnath, S. and Agarwala, S.**
- 132 Morphological process of podocyte development revealed by block-face scanning electron microscopy  
**Ichimura, K., Kakuta, S., Kawasaki, Y., Miyaki, T., Nonami, T., Miyazaki, N., Nakao, T., Enomoto, S., Arai, S., Koike, M., Murata, K. and Sakai, T.**
- 143 Cell polarity defines three distinct domains in pancreatic  $\beta$ -cells  
**Gan, W. J., Zavortink, M., Ludick, C., Templin, R., Webb, R., Webb, R., Ma, W., Poronnik, P., Parton, R. G., Gaisano, H. Y., Shewan, A. M. and Thorn, P.**
- 152 Applied stretch initiates directional invasion through the action of Rap1 GTPase as a tension sensor  
**Freeman, S. A., Christian, S., Austin, P., Lu, I., Graves, M. L., Huang, L., Tang, S., Coombs, D., Gold, M. R. and Roskelley, C. D.**
- 164 The cytostome–cytopharynx complex of *Trypanosoma cruzi* epimastigotes disassembles during cell division  
**Alcantara, C. de L., Vidal, J. C., de Souza, W. and Cunha-e-Silva, N. L.**
- 177 Deep nuclear invaginations are linked to cytoskeletal filaments – integrated bioimaging of epithelial cells in 3D culture  
**Jorgens, D. M., Inman, J. L., Wojcik, M., Robertson, C., Palsdottir, H., Tsai, W.-T., Huang, H., Bruni-Cardoso, A., López, C. S., Bissell, M. J., Xu, K. and Auer, M.**
- 190 Increased ROS production in non-polarized mammary epithelial cells induces monocyte infiltration in 3D culture  
**Li, L., Chen, J., Xiong, G., St Clair, D. K., Xu, W. and Xu, R.**

- 203** Comparison of cancer cells in 2D vs 3D culture reveals differences in AKT–mTOR–S6K signaling and drug responses  
**Riedl, A., Schleder, M., Pudelko, K., Stadler, M., Walter, S., Unterleuthner, D., Unger, C., Kramer, N., Hengstschläger, M., Kenner, L., Pfeiffer, D., Krupitza, G. and Dolznig, H.**
- 219** Pax8 controls thyroid follicular polarity through cadherin-16  
**Koumariou, P., Gómez-López, G. and Santisteban, P.**
- 232** Ultrasound patterning technologies for studying vascular morphogenesis in 3D  
**Comeau, E. S., Hocking, D. C. and Dalecki, D.**
- 243** ZO-1 interactions with F-actin and occludin direct epithelial polarization and single lumen specification in 3D culture  
**Odenwald, M. A., Choi, W., Buckley, A., Shashikanth, N., Joseph, N. E., Wang, Y., Warren, M. H., Buschmann, M. M., Pavlyuk, R., Hildebrand, J., Margolis, B., Fanning, A. S. and Turner, J. R.**
- 260** Three-dimensional imaging of the intracellular assembly of a functional viral RNA replicase complex  
**Fernández de Castro, I., Fernández, J. J., Barajas, D., Nagy, P. D. and Risco, C.**
- 269** A toolbox to study epidermal cell types in zebrafish  
**Eisenhoffer, G. T., Slattum, G., Ruiz, O. E., Otsuna, H., Bryan, C. D., Lopez, J., Wagner, D. S., Bonkowsky, J. L., Chien, C.-B., Dorsky, R. I. and Rosenblatt, J.**
- 278** 3D correlative light and electron microscopy of cultured cells using serial blockface scanning electron microscopy  
**Russell, M. R. G., Lerner, T. R., Burden, J. J., Nkwe, D. O., Pelchen-Matthews, A., Domart, M.-C., Durgan, J., Weston, A., Jones, M. L., Peddie, C. J., Carzaniga, R., Florey, O., Marsh, M., Gutierrez, M. G. and Collinson, L. M.**
- 292** Shear-wave elasticity measurements of three-dimensional cell cultures for mechanobiology  
**Kuo, P.-L., Charng, C.-C., Wu, P.-C. and Li, P.-C.**

**TOOLS AND TECHNIQUES**