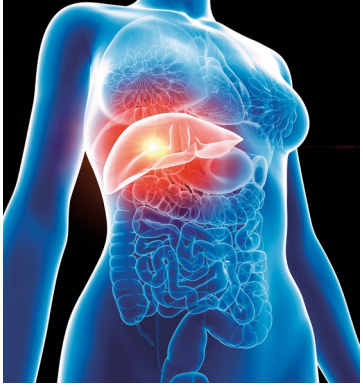

Credit: SCIEPRO/ SCIENCE PHOTO LIBRARY

found specifically at hypomethylated transposons. This was accompanied by a reduction in H3K27me3 levels at gene promoters, prominently of proliferation-related genes, many of which are differentially expressed between wild-type and *Uhrf1*^{hepKO} mice during liver regeneration.

Thus, in *Uhrf1*^{hepKO} livers, H3K27me3 is redistributed from pro-regeneration (and other) genes to hypomethylated transposons to compensate for their loss of silencing by DNA methylation, thereby potentiating liver regeneration. In the future, DNA methylation-targeting drugs could be tested for their ability to increase the regenerative capacity of the liver.

Eytan Zlotorynski

> “H3K27me3 is redistributed from … genes to hypo-methylated transposons to compensate for their loss of silencing”

ORIGINAL ARTICLE Wang, S. et al. Epigenetic compensation promotes liver regeneration. *Dev. Cell* **50**, 43–56 (2019)

over time, effectively capturing functional restriction as it occurs during development. Analysis of the phylogenetic tree also showed that the extra-embryonic endoderm and the embryonic endoderm displayed an unexpectedly close ancestry, despite originating from the hypoblast and embryo-restricted epiblast, respectively; these data shed new light on the developmental relationship between tissues.

Finally, the phylogenetic tree enabled the authors to estimate the number of progenitors that constitute the early embryo.

These findings, coupled with the recorder having the capacity to produce mice that generate indels into adulthood, indicate that this molecular recorder will be an invaluable tool for studying mammalian development.

Katharine H. Wrighton

> “a CRISPR–Cas9-based ‘molecular recorder’ that, in mice, provides information on both cell state and cell lineage”

ORIGINAL ARTICLE Chan, M. M. et al. Molecular recording of mammalian embryogenesis. *Nature* https://doi.org/10.1038/s41586-019-1184-5 (2019)

FURTHER READING Pijuan-Sala, B., Guibentif, C. & Göttgens, B. Single-cell transcriptional profiling: a window into embryonic cell-type specification. *Nat. Rev. Mol. Cell Biol.* **19**, 399–412 (2018)

Journal Club

THE RISE OF A FORGOTTEN MODEL

In 1980, Graeme Mitchison (1944–2018) published a mathematical model of hormone movement through plant tissues. The model proposed a mechanism whereby feedback on directional transport can lead to the formation of discrete strands of transport from a diffusive flow. Such a process of canalization can be seen in plant vascular tissues. Nothing was known about the underlying molecular mechanisms that induce directional transport in plants at the time, but thorough analysis and understanding of the dynamic properties described by the equations enabled Mitchison to make precise predictions about what elements are required to generate canalization.

Back then, the model received little attention: Graeme told me that he moved on to other problems as only very few people seemed to care about his model. About 15 years later, PIN proteins were identified as being involved in the directional transport of auxin. When the polarized membrane localization of PIN proteins was visualized in different vascular tissues, it correlated strikingly well with the transport directions predicted in Mitchison’s model. After the discovery of the PIN proteins, Mitchison’s study and predictions have inspired a new generation of modellers aiming to connect auxin transport with PIN dynamics, and today experimental papers frequently cite the Mitchison model as a possible mechanism for canalization.

> “it shows the value of applying a rigorous analysis to the mathematical model and discussing the predictions in detail”

The strength of the paper lies not just in the novelty of the proposed mechanism describing a dynamic pattern, but also in the fact that it shows the value of rigorously analysing the mathematical model and discussing the resulting predictions in detail. For example, the analysis revealed how strong the feedback should be to have a canalization effect. Such measure of strength is a parameter that has recently been adapted for the model to be applicable to non-canalizing tissues. An unresolved aspect of Mitchison’s model is that it uses molecular flux across a membrane as a measure for feedback while experimental evidence for a flux-sensing mechanism in the auxin–PIN system is still missing. Computational researchers have followed up on this issue, and several new models, for how to generate ‘flux-correlated dynamics’ from standard mass action and auxin-gradient mechanisms, have been proposed.

It is an especially exciting time to be working in the life sciences, with access to rapidly advancing technologies and with a wide breadth of research fields now engaged in the pursuit of a quantitative understanding of complex biological systems. Mathematical models are used to formalize hypotheses for which mechanisms are sufficient to describe these systems. We have to appreciate that models of biology are still incomplete and maybe even wrong, but importantly, models can always be objectively challenged. Competing models are generated and history will tell which will be the most successful in pushing a research field forward.

Mitchison’s foundational work on the canalization model has inspired scientists for the past 40 years and continues to do so. It will be interesting to learn which models developed today will inspire the community and create a platform for future research.

Henrik Jönsson
Sainsbury Laboratory, University of Cambridge, Cambridge, UK
e-mail: henrik.jonsson@slcu.cam.ac.uk

The author declares no competing interests.

ORIGINAL ARTICLE Mitchison, G. J. A model for vein formation in higher plants. *Proc. R. Soc. Lond. B* **207**, 79–109 (1980)