cells is currently only a structural feature, and so the next challenge will be to use it for a specific function. The possibilities are endless. With some optimization, one could imagine the sequestered DNA serving as a useful starting point for gene circuits or IVTT reactions, for example.

Living cells divide to reproduce, which requires each cell to change shape before splitting into two. Much work is going on to achieve the division of artificial cells consisting of membrane-bound vesicles, with many research groups investigating the use of proteins from the cytoskeleton (see refs 8–10, for example) — the network of structural filaments that gives a cell its shape. However, it has proved more difficult to change the shape of coacervates[11].

"The artificial cells morphed over time into an asymmetrical shape reminiscent of amoeba."

Xu *et al.* show that actin, a cytoskeleton protein, can be polymerized enzymatically in the 'cytoplasm' of their artificial cells to produce a filamentous network. However, the overall morphology of the artificial cells remained spherical during this process. Intriguingly, the authors then encapsulated living bacteria inside the coacervates, and observed that the artificial cells morphed over time into an asymmetrical shape, reminiscent of that of natural cells such as amoeba. Although visually exciting, it is hard to see for now how this shape change might lead the way to artificial cell division.

A major drawback of Xu and colleagues' seemingly straightforward approach for using living systems as the basis for artificial cells is that all life forms contain many unknowns. Even the genome of the 'minimal cell' reported[12] in 2016 — which was engineered to contain only the genes thought to be essential for life — has a substantial fraction (about 30%) whose function is unknown, and bacterial cells are more complex than that. To build a fully controllable artificial cell, it will be necessary to identify the constituent parts needed and to understand how they interact with each other. For now, this work intriguingly demonstrates that biochemistry can function in conditions different from those found in natural cells.

The combinations of living and artificial cells reported by Xu *et al.* should make us all ponder, 'what is life?' Scientists typically use a reductionist approach that defines living things as those that have specific characteristics — such as cellular and subcellular compartmentalization, metabolism, information storage and processing, and regenerative capabilities[13]. Several types of artificial cell have emulated a few of these hallmarks[14]. However, if life is an emergent property that arises from complex network systems[15], then artificial cells must be able to integrate and connect many more of the characteristics just mentioned.

Xu and colleagues have provided a platform that might achieve this. Their current system integrates seven attributes of living cells: an outer membrane; a crowded interior; the ability to carry out cascades of enzymatic reactions; protein-synthesis capabilities; impressive structural organization with diverse subcompartments; a primitive cytoskeleton; and the ability to adopt asymmetric cellular shapes. But a truly living system has yet to emerge from the test tube — the reported artificial cells are the equivalent of cell-like automatons. Nevertheless, the new findings are an important step forwards in this field, demonstrating the power of coacervates to localize and integrate diverse biomaterials, including living cells, to make artificial cells. The next challenge is to make progressively interconnected networks that close the gap between artificial and living cells.

N. Amy Yewdall is at the Institute for Molecules and Materials, Radboud University, Nijmegen 6500 GL, the Netherlands.
e-mail: amy.yewdall@ru.nl

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Cancer

Human origins of medulloblastoma tumours

Timothy N. Phoenix

How certain subgroups of a childhood brain tumour called a medulloblastoma arise has been unclear. Evidence now implicates a cell type found only in developing human brains as the originator of these tumours. **See p.1012 & p.1021**

A brain tumour called a medulloblastoma is a relatively common type of childhood cancer, and encompasses four distinct subgroups[1]. The genetic causes and cellular origin have been identified for two of these subgroups (called WNT and SHH, respectively, after the signalling proteins associated with these two categories)[2,3]. However, much less is known about the remaining two groups (termed group 3 and group 4), which account for most cases. Smith *et al.*[4] (page 1012) and Hendrikse *et al.*[5] (page 1021) provide now insights into the origin and causes of these subgroups.

Over the past decade, the use of DNA- and RNA-sequencing techniques to analyse large clinical-sample collections from people with cancer has identified characteristic patterns of genetic alterations, signalling-pathway changes and gene-expression signatures in tumours previously thought to be identical. A notable example of this is medulloblastoma, which was historically characterized as a single type of cancer, defined by its presumed location of origin (the brain region known as the cerebellum) and tumour-cell shape[6]. International research collaborations have since refined the genetic landscape of medulloblastoma, dividing the disease into its four subgroups[7].

The WNT and SHH subgroups are caused by genetic alterations that result in the hyperactivation of Wingless (WNT) and Sonic hedgehog (SHH) signalling pathways, respectively[7]. Although certain genetic alterations, such as extra copies of the *MYC* gene[8], are associated with group 3 and group 4 medulloblastoma, the underlying causes of many of these tumours have not been fully understood. Moreover, convergence in the gene-expression patterns for group 3 and group 4 medulloblastoma raise further questions about whether they have unique or shared origins[9,10].

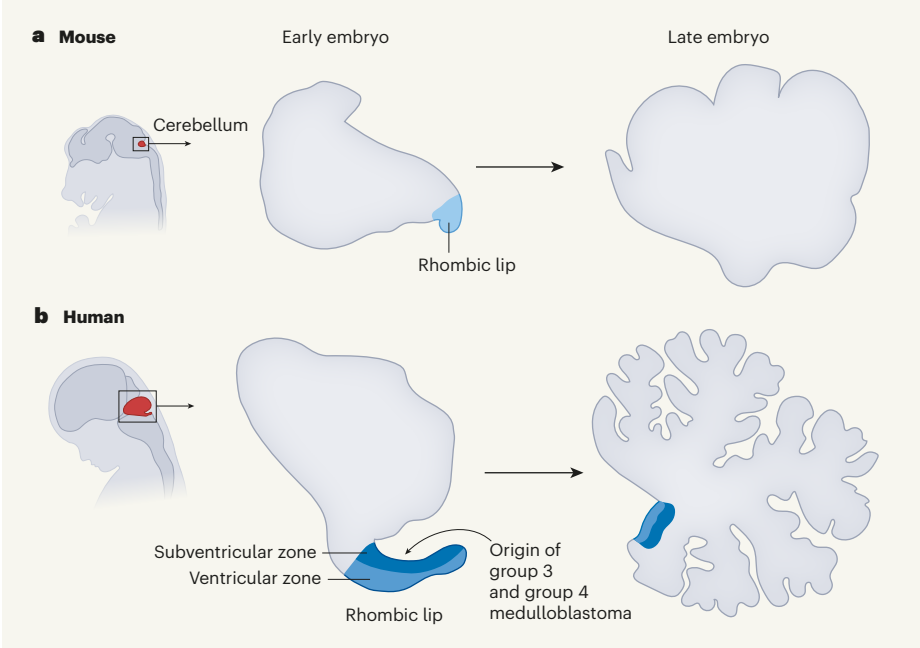

Figure 1 | The cellular origins of certain subgroups of medulloblastoma. A cancer called a medulloblastoma, which is associated with a region of the brain called the cerebellum, is divided into four subgroups. Smith *et al.*[4] and Hendrikse *et al.*[5] have identified a population of human cells — progenitor cells that can form neurons called unipolar brush cells (not shown) — as being the origin of two of these medulloblastoma subgroups (group 3 and group 4). **a**, **b**, Evidence for this was obtained using experimental approaches such as cross-species comparison of mouse and human cerebellar development. The authors report that these two types of medulloblastoma arise from cells found in a region of the developing human brain called the subventricular zone of the rhombic lip, which is adjacent to the ventricular zone. In contrast to human embryos, mouse embryos have a smaller and more-transient rhombic lip (RL) region that is not divided into two zones.

Smith *et al.* and Hendrikse *et al.* shed light on these questions by aligning genetic alterations and molecular signatures specific to the medulloblastoma subgroups with features unique to the development of the human cerebellum (Fig. 1). Using different experimental perspectives, the two papers propose that defects in the differentiation of a particular group of cells during human cerebellum development, namely, progenitor cells that give rise to a region called the rhombic lip subventricular zone (RL^{SVZ}), are the source of group 3 and group 4 medulloblastoma.

Using a gene-transcriptional atlas of single cells in the developing human cerebellum, Smith and colleagues discovered that transcription in group 3 and group 4 tumours matches the gene-expression pattern associated with progenitor cells in the RL^{SVZ} that give rise to a group of neurons called unipolar brush cells. In addition, some group 3 medulloblastomas also expressed genes encoding photoreceptor proteins. This is a surprising finding because such expression was not thought to be a hallmark of the developing or adult cerebellum. However, the authors show that these photoreceptor genes are indeed normally expressed by progenitors of unipolar brush cells in the human RL^{SVZ}, indicating that their expression is not aberrantly switched on as a consequence of cancer-associated abnormalities. Furthermore, when Smith *et al.* examined mutated genes associated with group 3 and group 4 medulloblastoma using various sequencing techniques, they found that such signatures specifically matched transcription patterns in the human RL^{SVZ}. This finding suggests a direct link between RL^{SVZ}-cell-type-specific gene activity and why these genes are affected in group 3 and group 4 medulloblastoma.

Hendrikse and colleagues took a different route. They examined gene mutations in group 3 and group 4 tumours, and identified recurrent examples of a type of change, called a loss-of-function mutation, in genes encoding members of, or interacting proteins associated with, the CBFA complex, a protein complex that recruits proteins (described as epigenetic modifiers) that modify the complex of protein–DNA in the nucleus called chromatin. Such alterations might, in turn, regulate developmental programs during cell differentiation. The authors report evidence for the expression of *CBFA2T2*, a gene associated with the CBFA complex, in the RL^{SVZ}. Comparing single-cell transcriptional signatures in the developing human cerebellum with those in samples of medulloblastoma, Hendrikse *et al.* show that signatures for group 3 and group 4 medulloblastoma are most similar to those for progenitors of unipolar brush cells. Taking this evidence together, the authors postulate that the RL^{SVZ} is the cellular origin of group 3 and group 4 medulloblastoma, and that these tumours are driven by disrupted function of the CBFA complex.

Approaching from different directions, the two groups arrive at a similar conclusion. Their finding echoes previous work implicating more-differentiated types of unipolar brush cell on the basis of transcriptional comparisons between medulloblastoma and cells in the developing mouse cerebellum[9,10]. Why weren't progenitors of unipolar brush cells identified in those comparison studies? The two new papers point to species-specific differences, namely, the presence of the RL^{SVZ} in humans, greater persistence of proliferative progenitors of unipolar brush cells during human development, and transcriptional differences between human and mouse cells. Thus, both papers offer evidence to support the argument that the large population of progenitors of unipolar brush cells in humans poses a high risk to our species of the development of group 3 or group 4 medulloblastoma.

The two studies, along with a related paper just published[11], answer key questions about the origins of group 3 and group 4 medulloblastoma. However, other questions remain. It will be essential to determine the precise function of the CBFA complex in the differentiation of progenitors of unipolar brush cells, to confirm that disruption of this complex drives the development of these medulloblastoma subgroups. Previous work investigating SHH and WNT medulloblastoma used genetically engineered mouse models to identify and confirm the cellular origins of those tumours[2,3]. Species-specific differences highlighted by the authors of the two latest studies caution against such an avenue of research. Advances in systems that study human tissue using 3D tissue cultures called organoids present an attractive alternative approach. However, improved protocols for boosting the differentiation of cerebellum-specific cell lineages are needed to fully harness the power of this experimental platform.

Understanding the origin of these tumours could lead to the development of improved treatment strategies: one could imagine therapies targeting disrupted differentiation programs in the RL^{SVZ} caused by CBFA-complex mutations or higher-than-normal levels of expression of photoreceptor genes. Improved animal-model systems that recapitulate essential human-specific differences could also lead to new insights into these tumours. Furthermore, the authors' work might pave the way to improved screening approaches for individuals at high risk of cancer, to intercept tumours at early stages of development.

Every villain has an origin story, and medulloblastoma is no exception. Let's hope that these developments will lead to heroic success in providing clinical benefits.

Timothy N. Phoenix is at the James L. Winkle College of Pharmacy, University of Cincinnati, Cincinnati, Ohio 45267, USA, and at Cincinnati Children's Hospital Medical Center.
e-mail: phoenity@ucmail.uc.edu

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Astronomy

Outer regions of galaxy clusters host megahaloes

Kenda Knowles

Observations reveal the presence of large volumes of ionized gas surrounding four galaxy clusters. The properties of these 'megahaloes' are distinct from those of similar haloes near the clusters, implying different formation mechanisms. **See p.911**

Radio haloes are large sources of radio-frequency emission that are found at the centre of galaxy clusters. They are thought to be produced when electrons travelling at speeds comparable to that of light are accelerated by magnetic fields in the turbulence that arises when the clusters merge. The detection of haloes spanning areas of around one square megaparsec has grown substantially over the past decade[1], thanks in part to the increased sensitivity of the present generation of telescopes. But now, on page 911, Cuciti *et al.*[2] report large volumes of faint, diffuse radio emission — on a much larger scale — surrounding four known radio haloes. The findings suggest that electron-acceleration mechanisms occur much farther out in the cluster region than had been previously thought.

Synchrotron emission is the electromagnetic radiation that is produced when 'relativistic' charged particles (such as electrons moving at light speeds) are accelerated by magnetic fields (such as those in galaxy clusters). The electrons lose energy as they travel through the magnetic field, which means that there is a limited time in which their synchrotron emission can occur. This time, in turn, constrains the distances over which emission should be detected. So emission over longer distances signals the existence of some mechanism through which energy is distributed to the electrons that allows them to maintain their relativistic speeds. Synchrotron emission is referred to as the non-thermal component of the radiation observed in cluster radio haloes, to distinguish it from the thermal emission that emanates from the hot gas.

The energy delivered to the electrons is thought to be produced by turbulence in the cluster centre, driven by massive mergers of clusters. This is supported by the fact that radio haloes are found almost exclusively in clusters that are currently experiencing substantial merger activity (or have done so in the past few hundred million years)[3]. The strength of the synchrotron emission also correlates with the mass of the system, with more-massive clusters producing more-powerful haloes[4].

With the advent of next-generation radio telescopes, such as the pathfinder and precursor instruments associated with the ongoing construction of the Square Kilometre Array (SKA) in South Africa and Australia, a handful of perplexing cluster observations have arisen in the past five years[5–7]. These clusters host diffuse emission sources that do not conform to existing classifications for the morphology of these sources. A dedicated survey of 115 galaxy clusters[5], undertaken with the MeerKAT telescope in South Africa, has increased this handful sufficiently to prompt a possible revision of the classification system — and perhaps even to current theories.

In spite of these discoveries, the non-thermal component of emission from galaxy clusters has yet to be probed in the outer region of clusters. Cuciti *et al.* used the Low-Frequency Array (LOFAR) in the Netherlands to do just this, by searching for diffuse emission in 310 galaxy clusters. In four of the clusters, they noticed that previously identified radio haloes were embedded in much larger volumes of synchrotron-radiation-emitting material. The

From the archive

An ancient mystery about poisonous honey solved, and the rise of photography to document museum collections.

100 years ago

In the September issue of *Discovery*, Prof. W. R. Halliday, with the help of his colleague, Prof. McLean Thompson, has cleared up a difficulty unsolved by editors of Xenophon's "Anabasis." The historian describes how the retreating Greeks, when they arrived near Trebizond, ate some honey, with effects ranging from intoxication to insensibility. Some authorities have denied that poisonous honey was found ... but the writers now point out that there is no evidence to show that the breed of bees ... or the general climatic condition, was responsible ... When honey is produced in excess, and the floral parts fail to develop, there results an accumulation of by-products in which toxins abound. When the competition for nectar pollen is intense many insects develop a biting habit, piercing the tissues of plants in search of short-cuts to food supply, and this habit results in the formation of poisoned honey. The observation of Pliny that honey was poisonous in some seasons and not in others is thus proved to be accurate, and can be explained on scientific grounds.
From *Nature* 30 September 1922

150 years ago

Photographs from the Collections of the British Museum. Taken by S. Thompson — Among all the varied purposes to which the art of photography has been applied, there is perhaps none for which it has proved itself more valuable than for the reproduction of ancient works of art ... [T]he reproduction by the camera ... will give a more vivid and faithful idea of the original than any drawing by however skilful an artist ... It is with great satisfaction, therefore, that we see this series of nearly a thousand quarto photographs of objects in our national collections ... We ... hope that each local museum will have its objects photographed and ... made accessible to the public at a fixed moderate cost.
From *Nature* 26 September 1872