50 Years Ago

Despite some impressive demonstrations of root-pressure, 'pumping' or positive pressure is generally thought to be of little importance for the ascent of sap in trees … In ten species of palms at Calcutta I was able to detect and measure positive root-pressures throughout the year, sometimes enough to lift sap to heights exceeding that of the trees … The positive pressure exceeds the negative pressure considerably. It often exceeds the plant's needs … The distal part of a cut root of a fruited banana plant was seen to develop pressure. The plant was decapitated at 2.25 m. above ground-level, and the cut root reconnected with a rubber tube. Other agencies such as transpiration are probably less important than root pressure.
From *Nature* 21 October 1961

100 Years Ago

My attention has been directed to three elm trees at Ettington … which it is said have been "killed by wasps." It appears that the wasps were attracted by the sweetness of the sap, and attacked the trees in such swarms, and so drained them of sap, that the death of the trees seems imminent, all the leaves having gone yellow long before the usual time. I should be glad to know if others have noticed attacks on elm trees, and whether the averred sweetness of the sap is due to some previous degenerative change in the tissues of the tree, or whether wasps would attack a normal tree if they could get access to the sap. The elms are all three comparatively young trees, and belong to the common variety. My informant tells me that he has previously noticed the same thing happen with an elm tree in one of his fields, which died the next winter.
From *Nature* 19 October 1911

species does not necessarily apply to all mammals, and especially not to humans. Despite great similarities in brain organization, there are also significant differences that could have profound functional consequences[10]. Obviously, one such difference is a decrease in adult neurogenesis and neuronal turnover that seems to have accelerated with primate evolution and that may be beneficial for human mental capabilities[11]. Examination of apes such as chimpanzees should answer the question of whether reduced neurogenesis in the adult SVZ is a uniquely human trait or a more general trend in hominoids. The present work also underscores the importance of considering species-specific differences in cellular mechanisms, and in their timing and function, in seemingly similar structures.

The general decrease in adult neurogenesis with vertebrate evolution is associated with a diminished capacity for neuronal replacement and regeneration[11]. Reprogramming of neural progenitors in the SVZ and redirecting of neuronal migration to achieve regeneration in injured brain areas are already proving to be formidable challenges in rodents. The present results[3], demonstrating the lack of significant neurogenesis and migration in the human SVZ beyond infancy, suggest that such strategies might be even more difficult to apply in our species. ■

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CHEMICAL BIOLOGY

Many faces of a cancer-supporting protein

The protein Hsp90 is a target of promising anticancer drugs. An analysis of the components of Hsp90 complexes in tumours reveals a path that may lead to predictive assays of drug sensitivity in cancer patients.

JOHN F. DARBY & PAUL WORKMAN

The protein Hsp90 is a molecular chaperone — it assists in the correct folding of other cellular proteins. Many of these Hsp90 'client' proteins are overexpressed and/or mutated in cancer and are involved in maintaining the cancerous state[1]. Hsp90 inhibition is therefore an attractive strategy for simultaneously blocking multiple abnormal pathways that are crucial for many tumour types[2]. Indeed, early clinical trials have confirmed the therapeutic potential of this approach. But understanding the mechanism that ensures selective targeting of tumour cells by Hsp90 inhibitors, and finding biomarkers to predict which cancers will be most sensitive to such treatment, has proved challenging. Writing in *Nature Chemical Biology*, Moulick *et al.*[3] use chemical proteomics — a combination of chemical precipitation and multi-protein profiling — to shed light on these questions.

There are some 20 Hsp90 inhibitors now in clinical trials. Their effects have been most impressive in breast cancers that overexpress a highly sensitive Hsp90 client, the HER2 oncoprotein, but that are resistant to the HER2-antibody drug trastuzumab[4]. They are also promising in non-small-cell lung tumours that express the mutated oncogenic protein EML4-ALK, a similarly sensitive Hsp90 client[5]. However, in other cancer types Hsp90 inhibition is less effective, despite the fact that the oncogenic constituents of such cancers are among Hsp90's clientele. The best path to obtaining approval for widespread clinical use of these inhibitors may therefore be to apply them in particular tumour subtypes that are driven by highly Hsp90-dependent oncoproteins[6]. To predict an individual patient's responsiveness, it will be crucial to define all of Hsp90's oncoprotein clientele and to understand the make-up and function of chaperone–client complexes, together with the molecular networks in which they are involved.

Large-scale genetic and messenger RNA/protein-profiling efforts have revealed that