

Market size, basic research and a wealth of experimental techniques provide the platform for an unprecedented opportunity to take the fruits of hearing research into the clinic, where it could benefit millions of people worldwide

Keynote review: The auditory system, hearing loss and potential targets for drug development

Matthew C. Holley

There is a huge potential market for the treatment of hearing loss. Drugs are already available to ameliorate predictable, damaging effects of excessive noise and ototoxic drugs. The biggest challenge now is to develop drug-based treatments for regeneration of sensory cells following noise-induced and age-related hearing loss. This requires careful consideration of the physiological mechanisms of hearing loss and identification of key cellular and molecular targets. There are many molecular cues for the discovery of suitable drug targets and a full range of experimental resources are available for initial screening through to functional analysis *in vivo*. There is now an unparalleled opportunity for translational research.

- ▶ There is a massive social and economic demand to develop therapeutic treatments for hearing loss. Deafness is one of the most widespread, costly and poorly understood disabilities in the world. It is also one of the most neglected. Its invisibility hides the suffering of many millions of people, who progressively lose their most important means of communication and who become socially isolated, especially in their later years.

In 2002, the World Health Organization (WHO) estimated that 250 million people have disabling hearing loss (www.who.int/pbd/deafness/en) and that two-thirds of them live in the developing world. The costs of communication disorders to the US economy have been estimated at US\$ 154–186 billion per year [1]. In 1997 the cost of noise-induced hearing loss alone was estimated to be between 0.2% and 2% of the gross domestic product. In the UK in 2002 this fraction was equivalent to US\$ 2.7–27 billion (Energy Information Administration, <http://eia.doe.gov/emeu/international/other.html>). The WHO described the scale of the problem, the primary causes and potential solutions in a series of conferences from 1994–1998 (www.who.int/pbd/publications/en/). It concluded that approximately 50% of hearing

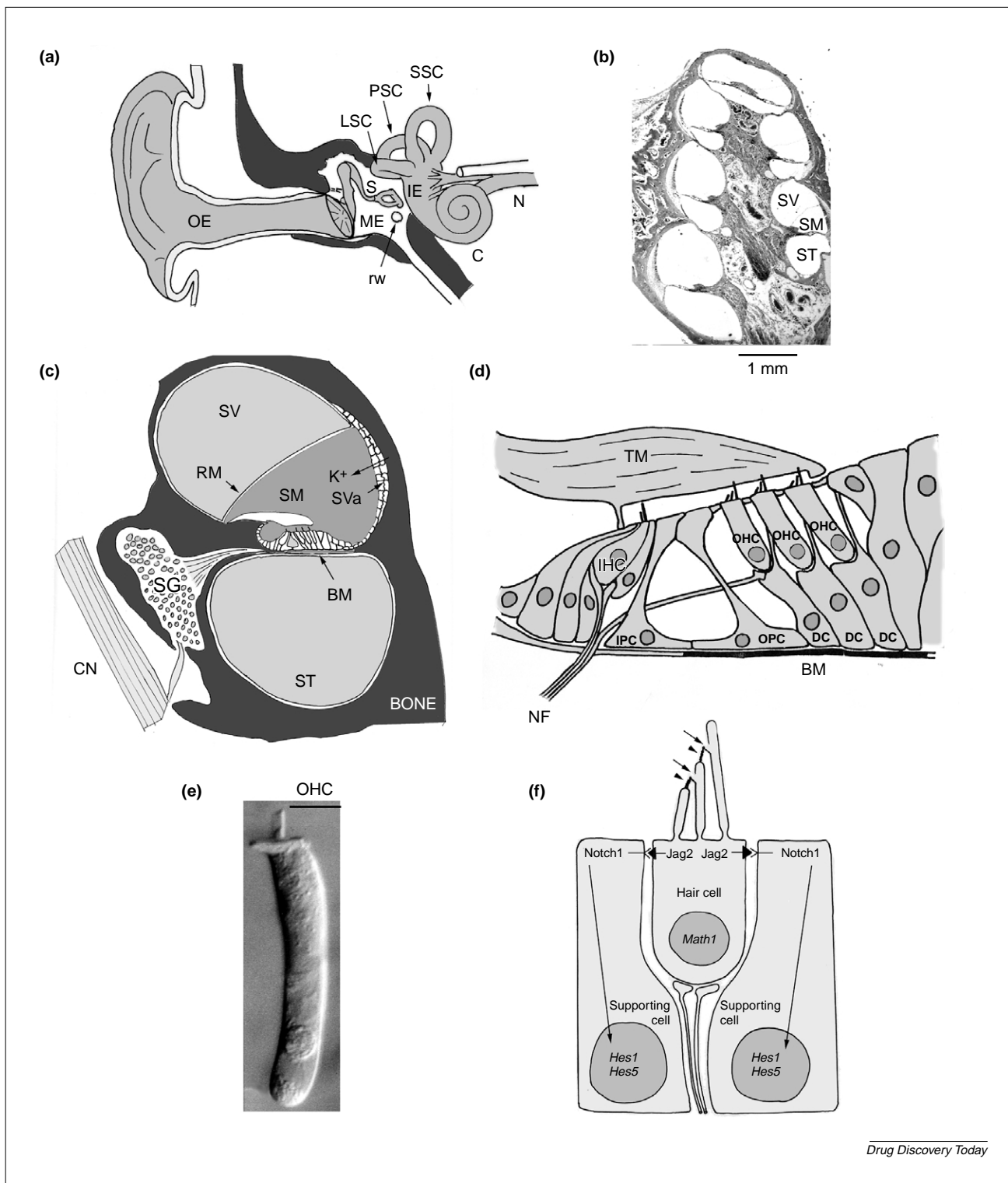
MATTHEW C. HOLLEY

Matthew Holley obtained his PhD in Zoology from the University of Oxford in 1983. He joined the hearing research field in 1986 at the University of Bristol, where he worked



on the mechanical properties of mammalian hair cells and supporting cells. He subsequently established some of the first cell lines from the mammalian cochlea and has combined *in vitro* preparations with gene array analysis to generate insight into mechanisms of development and regeneration. He has been Professor of Sensory Physiology at the University of Sheffield since 2001.

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loss is avoidable through careful management of noise exposure and of the administration of prescribed, ototoxic drugs. One of the key recommendations was investment in research, including translational research to bring some of the remarkable, recent developments in basic research closer to the clinic. Investment in hearing research has been extremely modest in comparison with the measured social and economic costs but it has yielded results to be envied by many other disciplines. Widespread research

activity has been underpinned by organizations, such as the National Institute for Deafness and other Communication Disorders (NIDCD) in the USA (www.nidcd.nih.gov), and large European consortia, such as GENDEAF (www.miteuro.org/gendeaf.htm) and the very recently launched EUROHEAR (www.eurohear.org). The global demand for therapeutic treatments is increasing dramatically with industrialization and lifespan. In developed countries the appetite for leisure noise among the young is expected to

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