CHEMISTRY

Perkin, the mauve maker

One hundred and fifty years ago this week, a teenager experimenting in his makeshift home laboratory made a discovery that in effect launched the modern chemicals industry. William Perkin was an 18-year-old student of August Wilhelm Hofmann at the Royal College of Chemistry in London, working on the chemical synthesis of natural products. In a classic case of serendipity, Perkin chanced on his famous 'aniline mauve' dye while attempting to synthesize something else entirely: quinine, then the only known remedy for malaria.

As a student of the renowned German chemist Justus von Liebig, Hofmann had made a name for himself by showing that a basic compound called aniline, obtained from coal tar, had the same properties as a compound distilled from raw, plant-derived indigo. Coal tar was the residue of coal-gas production, and there was intense interest in finding uses for the aromatic compounds, such as aniline, that could be extracted from it.

Working at home, Perkin tried to use an aniline derivative to make quinine by oxidation, based on the similarity of their chemical formulae (their molecular structures are very different). The reaction produced only a reddish sludge. But when the inquisitive Perkin tried the reaction using aniline instead, he got a black precipitate that dissolved in methylated spirits to give a purple solution. Textiles and dyeing being big business at the time, Perkin was astute enough to test the coloured compound on silk, which it dyed richly. Hitherto, almost all dyes were natural compounds extracted from plants and animals.

Boldly, Perkin persuaded his father and brother to set up a small factory with him to manufacture the dye, which he called mauve; the picture here is of a shawl, dyed with mauve, from 1862. The Perkins and others (including Hofmann) soon discovered a whole rainbow of aniline dyes, and by the mid-1860s aniline-dye companies included the nascent giants of today's chemicals industry, such as Bayer, Hoechst and BASF.

SCIENCE MUSEUM

Philip Ball

ion is not bound by carbonyl oxygens, as it would be in KcsA, because of a rearrangement in the backbone of the selectivity filter, presumably caused by the change of tyrosine (Y) in KcsA to aspartate (D) in NaK. The third and fourth ion-binding sites are structurally very similar to their counterparts in KcsA, but can bind to K^+ and Na^+ with virtually no rearrangements in the protein. These differences might make the NaK pore seem shorter in electrophysiological and flux studies than the K^+ channel pore[1].

Another intriguing finding in the NaK structure was the presence of a divalent binding site, capable of binding Ca^{2+}, at the extracellular entrance to the NaK selectivity filter. Although an extracellular Ca^{2+}-binding site has been proposed in many Ca^{2+}-permeable channels, this site has always been thought to involve the carboxylate of an acidic residue in the selectivity filter. Surprisingly, in the NaK structure this acidic residue, the aspartate, is facing away from the pore, and the binding site for Ca^{2+} is formed by backbone carbonyls of the glycine residues at the extracellular end of the selectivity filter sequence. In CNG channels, this acidic residue has also been proposed to be involved in regulating a number of permeation and blocking properties, including ion selectivity, divalent block, proton block and state-dependent tetracaine block[10]. Although the sequence similarity is weaker between CNG channels and voltage-gated Ca^{2+} and Na^+ channels (Fig. 2), a similar role for an acidic residue has been suggested in those channels[1].

The finding that the aspartic-acid residue in the NaK structure does not bind directly to the ions raises some interesting questions. Can the charge on this residue exhibit a through-space electrostatic interaction with ions in the pore? Do mutations of this residue alter the backbone structure and so indirectly alter ion-binding sites? Could the position of this acidic residue be different in open channels? And, is the NaK channel pore structure representative of eukaryotic CNG channels and voltage-gated Ca^{2+} channels? As always, X-ray crystallography has answered many questions with astonishing clarity, but there are yet more to be addressed. ■

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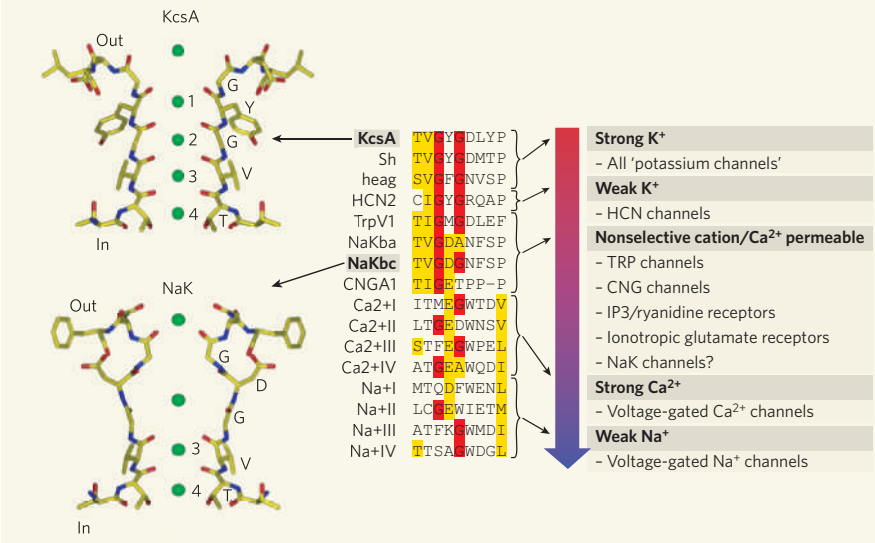

Figure 2 | Mechanism of ion selectivity. The amino-acid sequences from a range of ion channels (centre) show remarkable similarity in the region of the selectivity filter. Red highlights show the conserved glycines in the 'signature' sequence TVGYG found in the potassium ion channel KcsA. Yellow highlights show amino acids that are chemically similar. As the filter sequence becomes less conserved, the channels lose their selectivity for K^+ over Na^+ and become more permeable to Ca^{2+}. The structure of the nonselective cation channel NaK from *Bacillus cereus* has been solved by Jiang and colleagues[5]. Comparison of the selectivity filters of NaK and KcsA (left) provides structural clues to sodium-ion permeability.

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