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Wayne I. L. Davies

Editor PPT

Biography

- Wayne I. L. Davies received his PhD from Cambridge University, UK. Professionally linked to many internationally renowned research institutions, Wayne Davies is currently an Associate Professor at the School of Animal Sciences, University of Western Australia, Australia. His main research interests broadly encompass the molecular evolution and functional characterisation of gene families, and the mechanisms that regulate gene expression. Specifically, A/Prof. Davies investigates the evolutionary origins, molecular ecology, function and spectral tuning of photopigments that mediate chordate visual and non-visual light detection, and their phototransduction cascades. His work also extends to determining genetic mutations in retinal and neurological diseases. Other interests include tissue-specific regulation of ABC transporters, in particular the cystic fibrosis (CFTR) gene, novel mechanisms of gene regulation (e.g. post-transcriptional regulation and non-coding RNA networks of gene expression), and the phylogenetic relationships that exist between and across large protein superfamilies (e.g. GPCRs, ABC transporters, ion channels).

Research Interests

- Molecular evolution and functional characterisation of gene families, especially those involved in visual and non-visual photoreception, and the mechanisms that regulate gene expression.

Recent Publications

- McClements, M., **Davies, W.I.**, Michaelides, M., Young, T., Neitz, M., Maclaren, R.E., Moore, A.T. & Hunt, D.M. (2013) Variations in opsin coding sequences cause X-linked cone dysfunction syndrome with myopia and dichromacy. *Investigative Ophthalmology and Visual Science*. Epub ahead of print.

- McClements, M., **Davies, W.I.**, Michaelides, M., Carroll, J., Rha, J., Mollon, J.D., Neitz, M., Maclaren, R.E., Moore, A.T. & Hunt, D.M. (2013) X-linked cone dystrophy and colour vision deficiency arising from a missense mutation in a hybrid L/M cone opsin gene. *Vision Research.* Epub ahead of print.

- Shanks, M.E., Downes, S.M., Copley, R.R., Lise, S., Broxholme, J., Hudspith, K.A., Kwasniewska, A., **Davies, W.I.**, Hankins, M.W., Packham, E.R., Clouston, P., Seller, A., Wilkie, A.O., Taylor, J.C., Ragoussis, J. & Németh, A.H. (2013) Next-generation sequencing (NGS) as a diagnostic tool for retinal degeneration reveals a much higher detection rate in early-onset disease. *European Journal of Human Genetics* 21: 274-280.

- Aslam, S.A., **Davies, W.I.**, Singh, M.S., Charbel Issa, P., Barnard, A.R., Scott, R.A. & MacLaren, R.E. (2013) Cone photoreceptor neuroprotection conferred by CNTF in a novel *in vivo* model of battlefield retinal laser injury. *Investigative Ophthalmology and Visual Science*. 54: 5456-5465.

- Gerkema, M.P., **Davies, W.I.**, Foster, R.G., Menaker, M. & Hut, R.A. (2013) The nocturnal bottleneck and the evolution of activity patterns in mammals. *Proceedings of the Royal Society B Biological Sciences* 280: 1765.

- #Knott, B., **#Davies, W.I.**, Carvalho, L.S., Berg, M.L., Buchanan, K.L., Bowmaker, J.K., Bennett, A.T. & Hunt, D.M. (2013) How parrots see their colours: novelty in the visual pigments of *Platycercus elegans.* *Journal of Experimental Biology* 216: 4454-4461. #Joint first authorship.

- **Davies, W.I.** (2013) CFTR: The CF Gene and Its Regulation in Physiology and Disease. *Encyclopaedia of Life Sciences* (http://onlinelibrary.wiley.com/doi/10.1002/9780470015902 .a0022929/full). Invited Review.

- **Davies, W.I.** (2014) Challenges using diagnostic next-generation sequencing in the clinical environment for inherited retinal disorders. *Personalized Medicine* 11: 99–111. Invited Review.

Molecular Evolution

- Study of how genes and proteins evolve and how organisms are related based on their DNA sequence
- Molecular evolution therefore is the determination and comparative study of DNA and deduced amino acid sequences and how they change over long periods of time.
- Sequences from different organisms or populations are compared, using as a codon-matched alignment

- Partial DNA sequence alignment of the SWS1 opsin coding region identified in human and lamprey

```
Human      ATGAGAAAAATGTCGGAGGAAGAGTTTTATCTGTTCAAAAATATCTCTTC
Lamprey    ATG------TCCGGAGATGAAGAGTTCTACTTGTTCAAAAACATCTCCAA
           ***            ** ******** **  ********** *****

Human      AGTGGGGCCGTGGGATGGGCCTCAGTACCACATTGCCCCTGTCTGGGCCT
Lamprey    AGTGGGGCCTTGGGATGGCCCGCAGTTTCACATTGCCCCGAAATGGGCTT
           ********* ******** ** ****  ***********    ***** *

Human      TCTACCTCCAGGCAGCTTTCATGGGCACTGTCTTCCTTATAGGGTTCCCA
Lamprey    TCTACTTACAAGCCGCGTTCATGGGCTTCGTGTTCATATGTGGCACGCCA
           ***** * ***** ** *********   ** *** *    **    ***

Human      CTCAATGCCATGGTGCTGGTGGCCACACTGCGCTACAAAAAGTTGCGGCA
Lamprey    CTGAATGCCATCGTTCTGGTGGTCACCATTAAATATAAGAAGCTGCGGCA
           ** ******** ** ******* ***  *    ** ** *** *******

Human      GCCCCTCAACTACATTCTGGTCAACGTGTCCTTCGGAGGCTTCCTCCTCT
Lamprey    GCCACTCAATTACATATTAGTGAACATATCGGCGGCAGGTCTCGTGTTCT
           *** ***** *****  * ** *** * **    * ***  ** *  ***
```

* = identical nucleotide; - = indel (insertion or deletion)

Comparison of partial amino acid sequences of the SWS1 pigment identified in human and lamprey

```
Human      MRKMSEEEFYLFKNISSVGPWDGPQYHIAPVWAFYLQAAFMGTVFLIGFP
Lamprey    M--SGDEEFYLFKNISKVGPWDGPQFHIAPKWAFYLQAAFMGFVFICGTP
           *     ********** ******** **** ********** **  * *

                                        Site 86
Human      LNAMVLVATLRYKKLRQPLNYILVNVSFGGFLL
Lamprey    LNAIVLVVTIKYKKLRQPLNYILVNISAAGLVF
           *** *** *  ************** *  *
```

= identical nucleotide; - = indel (insertion or deletion)

- Comparison of the amino acid sequences can be used to investigate gene/protein evolution, however, they can be used to infer functional characteristics as well. For example, F86 in the lamprey SWS1 pigment confers ultraviolet sensitivity (<400 nm), but a substitution to L86 (as in the human opsin sequence) causes a spectral shift to violet sensitivity (> 400 nm).

- Considerations: which is better (amino acid sequence or DNA sequence) to study function? Which is better to study evolution, especially over long time periods where multiple substitutions at the same site might occur and confuse the study of evolutionary pathways?

- By comparing sequences, is it possible to calculate the rate of change that occur within a sequence? In other words how fast do changes occur within a gene.

- A number of different rate equations have been proposed that attempt to quantify the number of changes per unit time.

- How are number of changes estimated?

  For example, DNA substitution models:
- Jukes – Cantor Model (1969)
- Kimura Model (1980)
- Tamura Model (1992)
- Tavare's Generalised Time-Reversible (GTR) model (1986)

- Different proposed models of DNA substitution attempt to take into account changes that may have occurred that do not result in a net change. For example, a zero change of C to C may have arisen via C to T to C substitutions.

- Thus, the rates of change can be estimated, but are the rates the same for all nucleotides? Note, the third nucleotide of a codon is more like change (higher rate of change) than position 1 or 2.

- Amino acid comparisons minimise these issues, but there may be a significant loss of genetic information that might alter the resolution and branching of phylogenetic trees.

- Therefore, mutation rates are often NOT the same, although assumptions are made that greatly simply these potential hazards when generating basic phylogenetic trees.

- Rates may differ across different synonymous and non-synonymous sites.
- Protein evolutionary rates may differ depending on those that are under greater selective pressure (e.g. visual opsins vs housekeeping proteins).
- Organelle differences (e.g. mitochondrial vs nuclear DNA mutation rates).

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