



Sir Philip COHEN, PhD, Professor of Biology

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Background Information

Philip Cohen received his B.Sc (1966) and Ph.D (1969) from University College London and then spent two years as a postdoctoral fellow at the University of Washington, Seattle, USA. with Edmond Fischer (the 1992 Nobel Laureate for Medicine or Physiology). In 1971 he returned to the UK to become a Faculty member at the **University of Dundee, Scotland where he has worked ever since**. Philip has been a Royal Society Research Professor since 1984, Director of the Medical Research Council Protein Phosphorylation Unit since its inception in 1990, and is the Honorary President of the British Biochemical Society from 2006-2008. Philip is also the founder and Co-Director of the Division of Signal Transduction Therapy (DSTT) the UK's largest collaboration between a basic research institution and the pharmaceutical industry. It is widely regarded as a model for how industry and academia should interact, for which it received a Queen's Anniversary Award for Higher Education in 2006. For the past 40 years, Philip's research has been devoted to studying the role of protein phosphorylation in cell regulation and human disease, a process that controls almost all aspects of cell life. His contributions to this area, include working out over a 25 year period how insulin stimulates the synthesis of glycogen in muscle. Currently his laboratory is working on the signalling pathways that regulate the production of pro-inflammatory cytokines and interferons during bacterial and viral infection, research that is aimed at understanding how the uncontrolled production of these substances causes chronic inflammatory diseases, such as rheumatoid arthritis, asthma and septic shock.

Research

The major aim of my research is to dissect the signalling pathways that are activated during infection by bacteria and viruses, and to discover how they trigger the production of inflammatory mediators, such as pro-inflammatory cytokines and interferons. Understanding this system is critical, not only because of its importance in defence against infection, but also because its uncontrolled activation is a major cause of chronic inflammatory diseases, such as rheumatoid arthritis, inflammatory bowel disease, psoriasis and asthma, as well as septic shock.

The binding of bacterial and viral pathogens to Toll-like receptors (TLRs) in

immune cells, or interleukin-1 (IL-1) to the IL-1 receptor, recruits the signalling complex depicted in Fig 1. This triggers the IRAK4-catalysed activation of IRAK1, its release from the complex and binding to the E3 ubiquitin ligase TRAF6 with which it propagates the signal. The next step involves the formation of Lys63-linked polyubiquitin (K63-pUb) chains attached to TRAF6 and IRAK1 in which ubiquitin chains are linked to one another by isopeptide bonds formed between Lys63 of one ubiquitin and the C-terminal carboxyl moiety of the preceding ubiquitin [1, 5]. We recently showed that IRAK1 and IRAK4 phosphorylate Pellino isoforms *in vitro*, activating their latent E3 ubiquitin ligase activities. The Pellinos can then mediate the formation of K63-pUb-IRAK1 [2]. The formation of K63-pUb-TRAF6 is thought to be mediated by TRAF6 itself, although how this is initiated is unclear. The K63-pUb chains appear to act as scaffolds for the recruitment of protein kinases, such as TAK1 and IKK β (Fig 1). Our hypothesis is that the binding of TAK1 to K63-pUb-TRAF6, and IKK β to K63-pUb-IRAK1, co-localises these kinases to facilitate the TAK1-catalysed activation of IKK β [1]. Once activated, TAK1 and IKK β switch on several signalling pathways required to produce pro-inflammatory cytokines, such as TNF α (Fig 2). However, our other recent work has revealed that other activators of IKK β must be present in IL-1-stimulated fibroblasts [3]. The NEMO regulatory subunit of IKK β contains a polyubiquitin-binding domain that enables the recruitment of IKK β to K63-pUb-IRAK1 [1]. Intriguingly, the polyubiquitin-binding domain found in NEMO is present in four other human proteins. Discovering their roles in regulating the innate immune system, which is largely unknown, is one major aspect of our current work. We are also involved in dissecting the signalling pathways that activate two other IKK-related kinases, TBK1 and IKK β , which are required for the production of Type 1

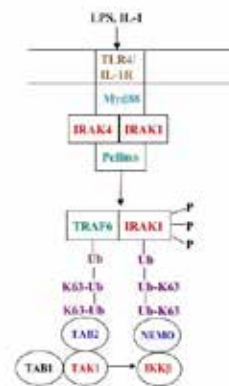
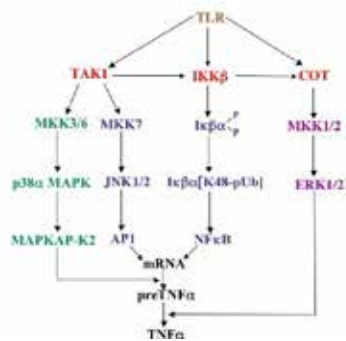


Figure 1. Early events in signalling by LPS and IL-1 / Figure 2. Signalling pathways activated by TAK1 and IKK β

The protein kinase TAK1 is required for the IL-1-induced activation of the protein kinases IKK β , p38 α MAPK and JNK. Once activated, IKK β activates the transcription factor NF κ B and the protein kinase COT. The activation of NF κ B is initiated by the phosphorylation of its inhibitory I κ B α subunit,

triggering the formation of K48-pUb-I κ B α and its degradation by the proteasome. JNK activates the transcription factor AP1 and, together with NF κ B, stimulates the transcription of genes encoding pro-inflammatory cytokines, such as preTNF α . In contrast, p38 α MAPK activates MAPKAP-K2, which stimulates translation of the mRNA encoding preTNF α . The role of COT (also called Tpl2) is to activate MKK1 and MKK2, which then activate ERK1 and ERK2. These MAP kinases stimulate the cell surface expression of preTNF α , where it is cleaved to the mature form and released into the blood [5].

Relevant recent references

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- [7] Yang, H-T, Cohen, P. and Rousseau, S. (2008) *Cellular Signalling* 20, 375-380. "IL-1 β -stimulated activation of ERK1/2 and p38 α MAPK mediates the transcriptional up-regulation of IL-6, IL-8 and GRO- α in HeLa cells."
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Publications

<http://www.ppu.mrc.ac.uk/research/?pid=1&sub1=publications>

Current Lab

http://www.ppu.mrc.ac.uk/research/?pid=1&sub1=current_lab

Lectures

Venue	Date
Proteomic Forum, Berlin	March 29 2009
The Proteomic Forum, Berlin	March 30 2009
The Society of Biomolecular Sciences Achievement Award Lecture, Lille, France	April 30 2009
BIO, Atlanta, USA	May 20 2009
Bloch Lecture, Louisville, Kentucky, USA	May 21 2009
Keynote Lecture International PhD student Cancer Conference, London	June 4 2009
President's Research Seminar Sloan-Kettering, New York	September 23 2009
GBM Symposium, Aachen, Germany	September 27 2009
Institute of Medical Sciences, Aberdeen	December 2 2009

Funding

Details: <http://www.ppu.mrc.ac.uk/research/?pid=1&sub1=Funding>

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Awards and Honours

- 2009** Achievement Award of the Society for Biomolecular Sciences
- 2008** Foreign Associate of the National Academy of Sciences, US
- 2007** Honorary Doctor of Laws, University of Dundee
- 2006** The Rolf Luft Prize, Stockholm, Sweden
- 2006** Queen's Anniversary Award for Higher Education
- 2006** Honorary President British Biochemical Society
- 2005** Honorary Doctor of Science, University of St Andrews, Scotland
- 2004** Royal Medal of the Royal Society of Edinburgh
- 2004** The Debrecen Award for Molecular Medicine, Hungary
- 2004** Honorary Doctor of Science, University of Debrecen, Hungary
- 2004** Honorary Doctor of Medicine, University of Linkoping, Sweden
- 2003** World's second most cited scientist in the fields of Biology and Biochemistry 1992-2003 (ISI, Philadelphia)
- 2003** Elected an Honorary member of The Biochemical Society
- 2002** Bristol-Myers Squibb Distinguished Achievement Award in Metabolic Research
- 2001** Sir Hans Krebs Medal, Federation of European Biochemical Societies
- 1999** 3rd most cited scientist based in the UK 1990-1999 (ISI, Philadelphia)
- 1999** Pfizer Innovation Award for Europe
- 1999** Honorary Doctor of Science, University of Strathclyde, Scotland
- 1998** Created Knights Batchelor in the Queen's Birthday Honours List
- 1998** Founder Fellow, Academy of Medical Sciences
- 1998** Honorary Doctor of Science. University of Abertay, Scotland
- 1998** Elected an Honorary Fellow of the Royal College of Pathologists
- 1998** Croonian Lecture of the Royal Society of London
- 1997** Datta Medal, Federation of European Biochemical Societies
- 1997** Louis Jeantet Prize for Medicine, Louis Jeantet Foundation, Geneva
- 1996** Elected a Fellow of the Royal Society of Arts
- 1996** Special Achievement Award, Miami Biotech Winter Symposium
- 1993** Bruce Preller Prize, Royal Society of Edinburgh
- 1993** Awarded the Dundee City of Discovery Rosebowl
- 1992** Elected a Fellow of University College London
- 1991** CIBA Medal and Prize of the British Biochemical Society Prix Van Gysel of the Belgian Royal Academies of Medicine
- 1990** Elected a Member of Academia Europaea
- 1989** Elected an Honorary Fellow of the Hannah Research Institute
- 1984** Elected a Fellow of the Royal Society of Edinburgh

- 1984** Elected a Fellow of the Royal Society of London
- 1982** Elected a Member of the European Molecular Biology Organisation
- 1977** Colworth Medal, British Biochemical Society
- 1977** Anniversary Prize, Federation of European Biochemical Societies

Information from Wikipedia

http://en.wikipedia.org/wiki/Philip_Cohen

Sir Philip Cohen [FRS](#) [FRSE](#) (born 22 July 1945) is a British researcher, academic and [Royal Medal](#) winner. During the 1990s he was Britain's third most cited professor^[1] (and the second most cited in the fields of biology and biochemistry)^[2] and has been described by Professor Garry Taylor of the [University of St Andrews](#) as "one of the world's top scientists".^[3] and by Professor Peter Downes as "arguably the UK's leading biochemist and an iconic figure in UK science".^[4] As of 2008 he has written over 470 peer-reviewed papers and given over 250 invited lectures in 33 countries,^[2] and has been repeatedly linked^[3]^[5] to a move of biotechnology companies to Dundee and the economic regeneration that came with it, to the point where 15% of the local economy is derived from biotech companies and their employees.^[5] His work has also seen Dundee attracting some of the world's best scientists, with over 1% of the world's most cited scientists residing in Dundee and fundraising of more than £35 million over the last 10 years to help attract them.^[5]

Early life and career

He was born in Middlesex,^[6] and after leaving [Hendon](#) County Grammar School he attended [University College London](#), where he was awarded a BSc in 1966 with first class honours and a PhD in 1969 under Michael Rosemeyer.^[4]^[7] After leaving UCL he spent two years at the [University of Washington](#) doing postgraduate work with [Edmond H. Fischer](#) before returning to Britain in 1971 to become a lecturer at the [University of Dundee](#), where he has remained for the last 37 years.^[7] He was made a reader in 1978 and gained a

personal chair in 1981.[6] In 1982 he was made a fellow of the [European Molecular Biology Organization](#), and in 1984 he became a [Royal Society](#) Research professor and elected a fellow of both the [Royal Society of Edinburgh](#) and [Royal Society](#).[2] In 1990 he was made Director of the Medical Research Council Protein Phosphorylation Unit[8], and a fellow of the [Academia Europea](#). In 1993 he was made a fellow of UCL and in the 1998 [Queen's Birthday Honours](#) was [knighted](#), served as a founding member of the [Academy of Medical Sciences](#) and was made an honorary fellow of the [Royal College of Pathologists](#).[4] In 2006 it was announced that Sir Philip Cohen would be taking over as president of the [Biochemical Society](#).[4]

Awards and recognition

He has received many awards for his work, including the 1992 Prix van Gysel of the Belgian Royal Academies of Medicine, a Special Achievement Award at the 1996 Miami Biotechnology Winter Symposium, the [Louis-Jeantet Prize for Medicine](#) in 1997, the Datta Medal of the [Federation of European Biochemical Societies](#) the same year[9] and a [Royal Medal](#) in 2008 for "his major contribution to our understanding of the role of protein phosphorylation in cell regulation".[10] He has also been given honorary DSc degrees from the universities of [Abertay](#), [Strathclyde](#), [Linköping](#) and [Debrecen](#).[4] He is now in the National Academy of Sciences.

References

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- ^ [a b c](#) ["BioDundee - Sir Phillip Cohen"](#). Retrieved on 2008-11-12.
- ^ [a b](#) ["Courier News Story - Honourary degrees span religion and science"](#). Retrieved on 2008-11-12.
- ^ [a b c d e](#) ["Biochemical Society Newsletter"](#). Retrieved on 2008-11-12.
- ^ [a b c](#) ["University of Dundee external relations: 40th Anniversary"](#). Retrieved on 2008-11-12.
- ^ [a b](#) ["Royal Society of Edinburgh"](#). Retrieved on 2008-11-12.
- ^ [a b](#) ["Philip Cohen - SCILIS - The Scottish Institute for Cell Signalling"](#). Retrieved on 2008-11-12.
- ^ ["MRC Protein Phosphorylation Unit"](#).

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