



*Dr Fu-Kien Lin, Director of Biomedical Sciences at Amgen, California, winner of the 1995 PhRMA 'Discoverer's Award'.*

remembered that Prof. Poggiolini disappeared in the summer of 1993 when called for questioning by Italian magistrates in connection with the drug corruption scandal that is still being investigated in Italy. He was subsequently traced to a Swiss clinic and extradited. When police

searched a house belonging to his wife in September 1993, they found a safe containing gold, currency, paintings and other valuables together with details of Swiss and Italian bank accounts totalling more than US\$15 million.

The charges against 67 defendants, including Prof. Poggiolini, relate to corruption and the illegal financing of political parties, including payments by pharmaceutical companies in return for quicker review of price increases and approval dossiers. The trial will take place in early 1996.

Speaking from prison, Prof. Poggiolini has implicated a number of leading pharmaceutical company executives, health officials and Vatican staff, claiming that he was an innocent victim. Those who have seen the manuscript have said that it contains a vigorous defence of his activities at the Ministry of Health and an attempt to rebut the charges laid against him. Prof. Poggiolini has always claimed that he managed to accumulate his fortune by prudent saving with the ultimate intention of setting up a research foundation on his retirement.

*David B. Jack*

## Progesterone and myelin synthesis

Progesterone plays a critical role in preparing the uterus to accept a fertilized ovum and in the maintenance and development of the fetus. It is an active component of birth control pills, and the progesterone receptor is the target for a 'morning after' contraceptive pill, RU-486. A French research group now reports that progesterone leads a double life. They believe it has a totally different, and so far poorly understood, role in the nervous system of both men and women as a regulator of the synthesis of myelin, the sheath that surrounds and insulates nerve cell axons.

The group, headed by Prof. Etienne-Emile Baulieu, Director of INSERM Unit 33 at the University of Paris and developer of RU-486, observed that progesterone is

present in high concentrations in sciatic nerve – in mice, some fivefold to tenfold the levels present in plasma.

Moreover, levels of progesterone in mouse sciatic nerve remain high even after castration and adrenalectomy, which causes disappearance of progesterone in the plasma. Schwann cells appear to be the source of the progesterone in nerve cell axons; cultured Schwann cells synthesize progesterone from radiolabelled precursors. The researchers found that oligodendrocytes also synthesize progesterone. Baulieu and coworkers reported their findings at the Fifth International Congress on Hormones and Cancer, held in September in Quebec City, Canada, and in *Science* (1995) 268, 1500–1503.

Schwann cells and oligodendrocytes both produce myelin; Schwann cells in the peripheral nervous system and oligodendrocytes in the central nervous system. According to Prof. Baulieu, it was natural to guess that progesterone would influence myelin biosynthesis. To test the idea, the researchers first destroyed a section of the sciatic nerve in male rats by freezing. Then they measured progesterone levels in the regenerating nerve and studied the effects of progesterone inhibitors and exogenous progesterone on myelin synthesis. They found that there is an increase in endogenous progesterone in the nerve during regeneration, and that the progesterone inhibitors trilostane and RU-486 reduced the layer of myelin in regenerated axons. When the researchers added progesterone simultaneously with trilostane, the thickness of myelin was much greater than in the control tissues.

At the Quebec congress, Prof. Baulieu's group reported that progesterone induces the *Krox20* gene in nerve cells. This gene codes for a transcription factor essential for nerve cell myelination. They also reported that progesterone triggers a rapid influx of  $Ca^{2+}$  into the Schwann cells and the activation of mitogen-activated protein kinase.

According to Greg Lemke, Professor of Neurobiology at the Salk Institute in La Jolla, California, "this work nails down a role for progesterone in development independent of its role as a sex steroid and may be of clinical importance". Lemke considers the inhibitor experiments to be very convincing, especially the significantly increased level of myelination observed when progesterone was added with the inhibitors.

Work is currently underway in Prof. Baulieu's laboratory to identify derivatives of progesterone that can reach the nerve and stimulate myelination without exerting a sex hormone action, according to co-author Dr Yvette Akwa (Scripps Research Institute, La Jolla, CA, USA). Such compounds would have obvious applications in testing the effects of progesterone on myelination in animal models of multiple sclerosis and other demyelinating diseases.

*Robert W. Wallace*