Cover Story

The GFP Story – Of men left in the dark

By N Rangarajan

The month of October holds a special place in any scientist's calendar. It is in this month that the Royal Swedish Academy of Sciences, in collaboration with other institutes, announces the Nobel Prizes for the year. And the deserving (did someone say lucky?) awardees are instantaneously catapulted into global limelight. The thought itself is funny - someone who remained largely unknown to a whopping majority of earthlings is suddenly looked upon as the epitome of scientific prowess. Documentaries are made, articles appear in newspapers, on coffee table journals; interviews are published – all this in a bid to understand and bring to public notice, the exploits of the chosen few. Nothing has changed this year.

Here, we attempt to bring to light two efforts that have been crucial to the development of the Green Fluorescent Protein (better know in biochemical circles as the GFP) as a tracer in biotechnology. No, this article isn't another eulogy of this year's Nobel winners in Chemistry. On the contrary, we choose to dwell upon two researchers who were, for some reason, ignored by the Nobel committee while deciding the awardees for this year's Prize.

Osamu Shimomura rose quite brilliantly from being blinded In Nagasaki to showing the rest of the world just what was behind the brilliant glow of jellyfish. Martin Chalfie probably sat in the right seminar and thereafter pursued his idea of fusing the gene encoding the GFP with others that code for common (and uncommon!) proteins. And Roger Tsien's childhood days in his basement laboratory seem to have had a purpose, when his fascination for colours translated into the development of a whole palette of fluorescent proteins.

The idea of using the GFP as a tracer molecule occurred first to Douglas Prasher in 1987, then a researcher at the Woods Hole Oceanographic Institution, Massachusetts. Prasher envisioned that it would be possible to incorporate the gene encoding the GFP into other genes and express this hybrid to get fluorescent biomolecules. In this way, the statics and dynamics of biomolecules could be tracked. Prasher found the gene that expressed the GFP and expressed it in bacteria. He reported his findings in a paper in Gene in 1992 [1]. He shared the GFP gene with Chalfie, who succeeded in incorporating it into E. coli. Both Chalfie and Tsien acknowledge Prasher's critical contribution. How-ever, as luck would have it, Prasher's NIH funds got exhausted soon after the 1992 paper, and after a couple of stints in other institutes, he quit science. He has since been driving for a car dealership in Alabama.

GFP applications received a major boost when Sergey Lukyanov's research group discovered GFP-like proteins in corals. They have since discovered GFPs in both fluorescent and non-fluorescent organisms as well as evolutionary distant species such as Cnidaria and Arthropoda. It may be safely concluded that the GFP evolved before the separation of these groups occurred. Lukyanov's group is currently extending the limits to the applications of this technology – from colour-changing proteins to fluorescent sensors to detect pH changes and charged species.

It remains to be seen as to how the Nobel affects research on GFP and its analogues. However, Prasher is almost certain to get back to research, a welcome sign indeed. It is now over to the Nobel lectures, to be held early in December.

Reference:

1. Prasher, D.C., Eckenrode, V.K., Ward, W.W., Prendergast F.G., Cormier, M.J., Primary structure of the Aequorea victoria green-fluorescent protein. *Gene*, **111(2)**, 229-233 (1992).

