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life
E - Newsletter
by Biological Sciences

From the Editor's Desk

(Ankita S. Nair)

Snuggling coyly in the southern ranges of the Sahyadri hills, one of the world's "Eco Hot-Spots", Amboli lies at an altitude of 690 meters above sea-level and is abounds in a variety of unique flora and fauna. It is a tranquil hill station on the Western Ghats, surrounded by thick forests and tree canopied hills, offering a bird's eye view of the Konkan coast. It offers a magnificent view of thousand waterfalls gushing down the hills.

The S.Y.BSc and T.Y.BSc students of Zoology had gone for a short study excursion to Amboli. At Amboli, we were greeted by the cool and invigorating climate which came as a respite from the city's harsh weather. Mornings in Amboli were very pleasant as the entire place was covered with thick fog. Evenings were accompanied by heavy showers of rain making the ambience cool and foggy. Once the rains subsided, we could spot many animals as they came out of their dwellings. As we ventured deep into the forests, we spotted animals like Indian Palm civet, Malabar Pit Viper, Wine snake, Red Helen butterfly and many more. Amboli's forests possess various species of amphibians, many of which are endemic. We were lucky to spot many amphibians like Amboli toad (*Xanthophryne tigerinus*), Common Indian toad (*Xanthophryne melanostictus*), Hemidactylus prashadi, Caecilian (*Ichthyophis*), Malabar Gliding frog (*Racophorus malabaricus*) Amboli bush frog (*Pseudophilautus amboli*), Bombay bush frog (*Raorchestes bombayensis*), Wrinkled frog (*Nyctibatrachus sp.*) to name a few.

Western Ghats is home to more than 5000 species of flowering plants segmented across 2200 genera and 217 families, of which one third is endemic and 140 mammal species of which 18 are endemic. There are about 457 species of birds, which attract many bird watching enthusiasts. It also supports around 265 species of reptiles and many amphibians. All in all it was a treat to our eyes to be able to get a glimpse of the rich biodiversity of Amboli.

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The Nobel Prize in Physiology or Medicine 2012 jointly to John B. Gurdon and Shinya Yamanaka.

"For the discovery that mature cells can be reprogrammed to become pluripotent"[1]

The Nobel Prize recognizes two scientists who discovered that mature, specialised cells can be reprogrammed to become immature cells capable of developing into all tissues of the body. Their findings have revolutionised our understanding of how cells and organisms develop.

John B. Gurdon discovered in 1962 that the specialisation of cells is reversible. In a classic experiment, he replaced the immature cell nucleus in an egg cell of a frog with the nucleus from a mature intestinal cell. This modified egg cell developed into a normal tadpole. The DNA of the mature cell still had all the information needed to develop all cells in the frog.

Shinya Yamanaka discovered more than 40 years later, in 2006, how intact mature cells in mice could be reprogrammed to become immature stem cells. Surprisingly, by introducing only a few genes, he could reprogram mature cells to become pluripotent stem cells, i.e. immature cells that are able to develop into all types of cells in the body.

Life – a journey towards increasing specialisation

All of us developed from fertilized egg cells. During the first days after conception, the embryo consists of immature cells, each of which is capable of developing into all the cell types that form the adult organism. Such cells are called pluripotent stem cells. With further development of the embryo, these cells give rise to nerve cells, muscle cells, liver cells and all other cell types - each of them specialised to carry out a specific task in the adult body. This journey from immature to specialised cell was previously considered to be unidirectional. It was thought that the cell changes in such a way during maturation that it would no longer be possible for it to return to an immature, pluripotent stage.

Frogs jump backwards in development

John B. Gurdon challenged the dogma that the specialised cell is irreversibly committed to its fate. He hypothesised that its genome might still contain all the information needed to drive its development into all the different cell types of an organism. In 1962, he tested this hypothesis by replacing the cell nucleus of a frog's egg cell with a nucleus from a mature, specialised cell derived from the intestine of a tadpole.

The egg developed into a fully functional, cloned tadpole and subsequent repeats of the experiment yielded adult frogs. The nucleus of the mature cell had not lost its capacity to drive development to a fully functional organism.

Gurdon's landmark discovery was initially met with scepticism but became accepted when it had been confirmed by other scientists. It initiated intense research and the technique was further developed, leading eventually to the cloning of mammals. Gurdon's research taught us that the nucleus of a mature, specialized cell can be returned to an immature, pluripotent state. But his experiment involved the removal of cell nuclei with pipettes followed by their introduction into other cells. Would it ever be possible to turn an intact cell back into a pluripotent stem cell?

A roundtrip journey – mature cells return to a stem cell state

Shinya Yamanaka was able to answer this question in a scientific breakthrough more than 40 years after Gurdon´s discovery. His research concerned embryonal stem cells, i.e. pluripotent stem cells that are isolated from the embryo and cultured in the laboratory. Such stem cells were initially isolated from mice by Martin Evans (Nobel Prize 2007) and Yamanaka tried to find the genes that kept them immature. When several of these genes had been identified, he tested whether any of them could reprogram mature cells to become pluripotent stem cells.

Yamanaka and his co-workers introduced these genes, in different combinations, into mature cells from connective tissue, fibroblasts, and examined the results under the microscope. They finally found a combination that worked, and the recipe was surprisingly simple. By introducing four genes together, they could reprogram their fibroblasts into immature stem cells!

The resulting induced pluripotent stem cells (iPS cells) could develop into mature cell types such as fibroblasts, nerve cells and gut cells. The discovery that intact, mature cells could be reprogrammed into pluripotent stem cells was published in 2006 and was immediately considered a major breakthrough.

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From surprising discovery to medical use

The discoveries of Gurdon and Yamanaka have shown that specialised cells can turn back the developmental clock under certain circumstances. Although their genome undergoes modifications during development, these modifications are not irreversible. We have obtained a new view of the development of cells and organisms.

Research during recent years has shown that iPS cells can give rise to all the different cell types of the body.

These discoveries have also provided new tools for scientists around the world and led to remarkable progress in many areas of medicine. iPS cells can also be prepared from human cells.

For instance, skin cells can be obtained from patients with various diseases, reprogrammed, and examined in the laboratory to determine how they differ from cells of healthy individuals. Such cells constitute invaluable tools for understanding disease mechanisms and so provide new opportunities to develop medical therapies.

Robert J. Lefkowitz - Howard Hughes Medical Institute and Duke University Medical Center, Durham, NC, USA.

Brian K. Kobilka - Stanford University School of Medicine, Stanford, CA, USA.

"For the studies of G-protein–coupled receptors"[1]

Smart receptors on cell surfaces

Your body is a fine-tuned system of interactions between billions of cells. Each cell has tiny receptors that enable it to sense its environment, so it can adapt to new situations. Robert Lefkowitz and Brian Kobilka are awarded the 2012 Nobel Prize in Chemistry for ground-breaking discoveries that reveal the inner workings of an important family of such receptors: G-protein–coupled receptors.

For a long time, it remained a mystery how cells could sense their environment. Scientists knew that hormones such as adrenalin had powerful effects: increasing blood pressure and making the heart beat faster. They suspected that cell surfaces contained some kind of recipient for hormones. But what these receptors actually consisted of and how they worked remained obscured for most of the 20th Century.

Lefkowitz started to use radioactivity in 1968 in order to trace cells' receptors. He attached an iodine isotope to various hormones, and thanks to the radiation, he managed to unveil several receptors, among those a receptor for adrenalin: β-adrenergic receptor. His team of researchers extracted the receptor from its hiding place in the cell wall and gained an initial understanding of how it works.

The team achieved its next big step during the 1980s. The newly recruited Kobilka accepted the challenge to isolate the gene that codes for the β-adrenergic receptor from the gigantic human genome. His creative approach allowed him to attain his goal. When the researchers analyzed the gene, they discovered that the receptor was similar to one in the eye that captures light. They realized that there is a whole family of receptors that look alike and function in the same manner.

Today this family is referred to as G-protein–coupled receptors. About a thousand genes code for such receptors, for example, for light, flavour, odour, adrenalin, histamine, dopamine and serotonin. About half of all medications achieve their effect through G-protein–coupled receptors.

The studies by Lefkowitz and Kobilka are crucial for understanding how G-protein–coupled receptors function. Furthermore, in 2011, Kobilka achieved another break-through; he and his research team captured an image of the β-adrenergic receptor at the exact moment that it is activated by a hormone and sends a signal into the cell. This image is a molecular masterpiece – the result of decades of research.

[1] http://www.nobelprize.org

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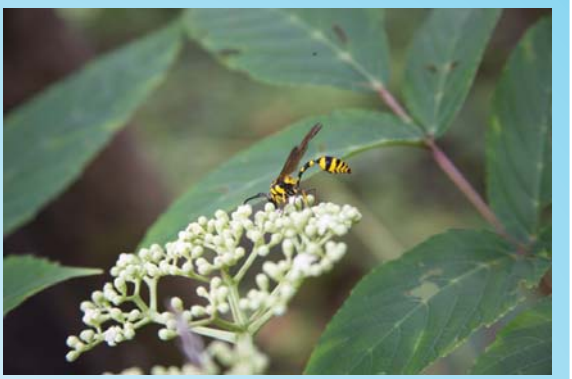
PHOTO GALLERY









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