Regulation role

The discovery of microRNA changed the understanding of gene regulation

This year's Nobel Prize in Physiology, or Medicine, awarded to Victor Ambros and Gary Ruvkun, is for their discovery of microRNA, small RNA regulators of gene expression in eukaryotes, and its role in gene regulation after transcription — the process of making an RNA copy (messenger RNA or mRNA) of a gene's DNA sequence — and before cellular machinery is activated for protein production. Before the discovery of microRNAs and their role in gene regulation, it was believed that gene regulation was limited to specialised proteins called transcription factors, which bind to specific regions in DNA and determine which mRNAs are produced. In 1993, using 1 mm long mutant roundworms called *C. elegans*, the winners of this year's Nobel provided proof that gene regulation is not confined to transcription factors. Instead, regulation by microRNAs occurs at a later stage in the process of gene expression, post-transcription. Despite these seminal findings, it was initially thought that this unusual mechanism of gene regulation was peculiar to *C. elegans* and not relevant to more complex organisms, including humans. However, the discovery of another microRNA encoded in a gene present in all organisms indicated that microRNA's role in gene regulation extends beyond roundworms. By 2001, microRNAs were found to be abundant in invertebrates and vertebrates, with some highly conserved across species, suggesting that "microRNA-mediated post-transcriptional regulation is a general regulatory function". As per current knowledge, the human genome codes for over 1,000 microRNAs.

Cancer, diabetes and autoimmune diseases are associated with dysregulated microRNA expression. In the case of cancer, dysregulation may include amplification or deletion of microRNA genes, abnormal transcriptional control of microRNAs, and defects in the microRNA biogenesis machinery. Studies have shown that dysregulated microRNAs affect the biological capabilities that cancer cells acquire during tumour development, including sustaining proliferative signalling, resisting cell death, and activating processes that allow cancer cells to spread in the body. Preliminary studies have also indicated that certain microRNAs can serve as potential biomarkers for human cancer diagnosis, prognosis, and therapeutic targets. It is now known that beyond perturbing immune responses, disruption and dysfunction of microRNAs can initiate the production of autoantibodies and contribute to the pathogenesis of autoimmune diseases, including rheumatoid arthritis and multiple sclerosis. Several microRNA-associated diagnostic biomarkers have already been developed and used clinically, though they have yet to be commercialised. Likewise, candidate drugs targeting microRNAs are currently being tested in clinical trials.