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► **COVER:** 'Signal, Response,' by Patrick Morgan, inspired by the review on p841.



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The first week of October saw outstanding contributions to the field of gene regulation amply rewarded in the shape of two Nobel Prizes. The studies that these awards celebrate highlight examples of two fundamental approaches to biological problems that should continue to inspire and motivate.

Roger Kornberg's Nobel Prize is a prime example of the fundamental importance of cross-disciplinary research. In 2001, Kornberg's group solved the structure of RNA polymerase II, paving the way for many advances in understanding the transcription machinery. Questions have been raised about the awarding of this prize — in chemistry — for an advance that has such a clear biological focus. Nonetheless, it was the use of a hard-core chemistry method, X-ray crystallography, that was key to this achievement. This cross-pollination between chemistry and biology has a long history. The Nobel Prize that was awarded to Crick, Watson and Wilkins in 1962 for determining the structure of DNA also used X-ray crystallography. In that case, however, the prize was awarded for physiology or medicine.

This year's Nobel Prize in physiology or medicine illustrates another intellectual approach that characterizes many significant breakthroughs — the desire to understand seemingly esoteric phenomena. Craig Mello and Andrew Fire were rewarded for their work on what might have been considered a somewhat obscure biological issue. Working in the nematode *Caenorhabditis elegans*, Fire and Mello were intrigued to find that double-stranded RNA was a more potent inhibitor of gene expression than its single-stranded counterpart. Their investigations into a finding that could easily have been overlooked by researchers of a less curious nature catalysed an explosion of interest in the roles of small RNAs in gene regulation. The rest, as they say, is history.

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