

## ACCEPTANCE SPEECH

By

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Co-Winner of the 1996 King Faisal  
International Prize for Science  
(Biology)

Your Royal Highness Prince Sultan ibn Abdul Aziz,  
Your Royal Highnesses,  
Your Excellencies,  
Distinguished Guests,

It is a great honour to be a recipient of The King Faisal International Prize for Science. King Faisal is remembered for his great benevolence and his devotion to the welfare of others. As scientists, we are motivated by a desire to understand the world we live in but I hope and believe that the knowledge we gain will lead to the betterment of mankind and thus that we are also working for the benefit of others. To have our efforts recognized is an enormous encouragement.

My own work, like that of my colleagues Drs. Blobel and Rothman, is concerned with the way in which cells secrete proteins. This is an intricate process of fundamental importance to all higher life forms. Secretory proteins are first inserted into a special compartment inside the cell and then moved through several more before finally being released to the outside. The compartments contain a mixture of proteins: those in transit to the surface and others, whose functions lie within the cell, which stay behind. As the proteins move through the cell they are continually sorted, thus ensuring that each one ends up in the right place. Our goal has been to identify the features that distinguish the different classes of protein and to understand the ways in which those features are recognized and sorting achieved. We have learned that few proteins have a fixed location—the apparent orderliness of a cell is like the order one sees in a library which remains tidy despite the fact that books are constantly being removed from the shelves and returned to

them. In the same way, proteins are constantly being lost from and returned to the various cellular compartments.

Although our desire is to understand how cells work, we also learn what happens when they do not work properly. Many inherited diseases, such as cystic fibrosis, are a consequence of particular proteins failing to follow the secretory pathway to the cell surface. In other diseases, toxic proteins enter cells and poison them, using the secretory pathway in reverse. Cholera toxin, for example, subverts the sorting system by imitating the features of a resident cellular protein, thereby ensuring that it is transported deep into the cells of the intestine where it does its damage. An understanding of such mechanisms may one day lead to improved treatments for these serious diseases.

Progress in science often depends on the efforts of many people, and I have had the pleasure of working with excellent colleagues over the years. These are too numerous to mention individually, but I would like to acknowledge two who have made particularly significant contributions: Michael Lewis, who was the first person to join my group and is with me still, and Sean Munro, my first graduate and now a close neighbour with a group of his own.

Throughout my independent career I have been fortunate enough to be supported by the Medical Research Council of Great Britain in a way that has allowed me to pursue the path of discovery wherever it leads. For a scientist this is a great privilege but there is also an obligation to use well the resources that are provided. It is thus very gratifying to see that our efforts have received international acclaim from such a prestigious organization as The King Faisal Foundation.

I would like to take this opportunity to express my gratitude to our hosts for their most generous hospitality. This is truly an occasion to remember.