Reining in the major global infectious diseases
Professor Sherry Mowbray’s research concerns some of the world’s most serious diseases, including malaria and tuberculosis. Malaria kills nearly a million people each year, and half the world’s population lives in high-risk regions. And it is estimated that every third person in the world is infected with tuberculosis, with one and a half million people dying from it annually. Furthermore, the problems are expected to get worse, as more and more pathogens become resistant to the drugs available now. This is an alarming trend, because one day we may no longer have any effective treatments left.

“The situation is serious and urgent. If we do not find solutions to the problems of pathogen resistance, we could die from everyday infections,” says Sherry Mowbray, “so we must not bury our heads in the sand.”

The medicines used to treat tuberculosis today were developed 50 years ago. Susceptible bacteria take 6-9 months to treat, but more resistant strains take up to 24 months, if the treatments work at all. As the drugs have a number of unpleasant side effects, getting patients to continue taking them for such a long period of time is a real challenge. This can make treatment unsuccessful, while encouraging resistance. The search for new drug candidates is therefore extremely important, but costly and time-consuming, with perhaps only five molecules from the many, many thousands investigated being viable drug candidates. And perhaps only one gaining FDA approval, explains Sherry Mowbray. Collaboration with other research groups, in Sweden and elsewhere, in academia and private enterprise, is critical in this detective work.

“Producing a new drug often takes more than ten years at an average cost of $2.6 billion. Finding fruitful collaborations is essential,” says Sherry Mowbray. She thinks this kind of research is interesting and exciting, and having the opportunity to think through key issues from different perspectives, with different knowledge and interests, is highly stimulating. But it is sometimes a challenge getting the teams to work optimally, and she likens it to herding cats.

Companies such as AstraZeneca and Sanofi have been important partners, and she also mentions very fruitful collaborative research in tuberculosis within the EU. By adopting a broad approach, they hope to understand more about the mechanisms behind infection, to be able to detect and evaluate several new drug candidates, and to identify new targets. Sherry Mowbray’s research team consists primarily of structural biologists, experts in determining how different proteins look at the molecular level. This helps them to connect the various structures to the proteins’ many different functions.

“We work in the early phase of drug discovery. After that, others need to take over. For example, clinical trials are carried out by others who are experts in that area,” says Sherry Mowbray.

The research team is also interested in a group of bacteria called the ESKAPE pathogens. These resistant bacteria cause the majority of the serious, sometimes fatal, infections that patients can acquire while in hospital. For pathogens to be active, they frequently require enzymes that are not found in humans. As in the studies with tuberculosis and malaria pathogens, the research team aims to establish how these enzymes look, enabling them to block the enzymes’ activity using small molecules called inhibitors. The hope is to create new and improved inhibitors, ones that can kill the relevant pathogens without harming the human body. Collaboration with chemists is always an important part of this research. Together, structural biologists and chemists can design compounds that are better inhibitors of the target enzyme, and hopefully have other desirable properties such as efficient uptake by the pathogen and low toxicity to the patient. The long-term goal is to find new drugs that will improve the lives of hundreds of millions of people. The discovery of a drug that is widely used in treating malaria shared the 2015 Nobel Prize in Physiology or Medicine.

“That was so exciting. It was exactly the sort of candidate we are looking for, giving us new treatments for a serious disease that afflicts humanity so severely,” she concludes.