AN AUDIENCE WITH…

Morgan Sheng

Vice President, Neuroscience, Genentech, South San Francisco, California, USA. Morgan Sheng started at Genentech in September 2008, having previously spent 14 years as a faculty member in the Boston area — first at Massachusetts General Hospital/Harvard Medical School and then at Massachusetts Institute of Technology, where he was Menicon Professor of Neuroscience in the Department of Brain and Cognitive Sciences and the Department of Biology. Before completing his Ph.D. in molecular genetics at Harvard University, he was a practising physician in London, UK.

When Genentech spun off Rinat Neuroscience in 2001, it seemed that the company did not wish to pursue neuroscience indications. What factors have contributed to Genentech's renewed interest in this area?

Around 10 years ago, Genentech felt that the main neuroscience indications were too poorly understood and not amenable to a biologics approach, so it was a strategic decision to focus efforts on cancer and spin off some neuroscience assets in Rinat Neuroscience.

There are three major reasons for Genentech's renewed interest in neuroscience. First, neuroscience has advanced to the point that the major unmet needs in neurological illnesses are becoming scientifically tractable. Second, Genentech has built up a world-class small-molecule drug discovery department and, clearly, if you want to develop treatments for the brain you need to develop small molecules in addition to large molecules. Third, the research leadership of Richard Scheller and Mark Tessier-Lavigne — who joined Genentech in 2001 and 2003, respectively — both have backgrounds in neuroscience (indeed, they are members of the US National Academy of Sciences in the neuroscience division). So, it's the combination of breaking science, Genentech's small-molecule capability and a strong expertise in-house that have reignited the interest of Genentech in Neuroscience.

Which areas of neuroscience does Genentech focus on and why?

We are currently focusing on neuro-degenerative diseases, such as Alzheimer's disease, Parkinson's disease and some of the less common neurodegenerations like amyotrophic lateral sclerosis (also known as Lou Gehrig's disease). There is a critical need in this area because no medicines are yet available that slow down or reverse the progression of these illnesses. We have interests in non-neurodegenerative indications as well.

What are the main challenges of developing innovative therapies for neuroscience indications?

The main challenge is that, despite scientific advances, we still understand little about how the brain works; therefore, unlike for cancer, for example, it is not that easy to identify the specific molecules and pathways to target. A second challenge is that there are few good animal models of neurological illnesses. The models are improving for some neurodegenerative diseases, for example Alzheimer's disease, but we need better models for Parkinson's disease. Consequently, the field is moving towards modelling specific endophenotypes, rather than whole disease states. The blood–brain barrier is another challenge because it prevents most drugs from getting into the brain — that applies to larger molecules like antibodies, as well as small molecules.

Diagnosis of neurological disease is also challenging as it is largely subjective, often grouping various heterogeneous diseases into one diagnosis. Moreover, the diagnostic criteria of some disorders can change substantially over time, as exemplified in the most recent revision of the Diagnostic and Statistical Manual of Mental Disorders.

Finally, clinical trials in neurological illnesses are difficult. In Alzheimer's disease, for example, because the disease progresses slowly, the clinical trials need to run for 18 months or more to show a disease modification outcome. Of course there is a major drug safety issue too, because central nervous system (CNS) disorders are typically chronic conditions requiring long-term treatment.

What are the advantages of addressing those challenges at Genentech?

Genentech is oriented to basic science. We try to understand the mechanisms of a disease and then, from that basis, develop a drug. We have excellent connections with academia, partly because of our own backgrounds, so we know what is going on at the cutting edge of neuroscience, and we also pursue cutting-edge science in-house. Researchers are attracted to Genentech because there is an academic culture that encourages them to publish. As a result, we get creative thinkers who love doing science. Most big pharmaceutical companies are more removed from basic research. They learn what is going on and react to it — we try to drive it.

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Has Roche's recent acquisition of Genentech provided new resources and networks that could help you to achieve the goals of the neuroscience research programme and, if so, how?

Genentech Research is independent of the rest of Roche in terms of research projects and research directions. However, obviously there are some synergies from the merger. Roche has a vibrant CNS unit based in Basel, Switzerland, and we can certainly benefit from Roche's worldwide presence and long experience in CNS drug development. We also are interested in diagnostics because, like every other kind of medicine, neurological treatments will need to be tailored to individuals. Roche has terrific resources in that area, such as expertise in genetic tests and imaging and protein biomarkers, which will complement ours. I think it is a win–win situation, with the advantage of intellectual independence.