



animal testing, rein in ballooning drug development costs and put Japan at the forefront of highly competitive global efforts to understand the genetic background of adverse drug reactions.

NIBIO is creating a cell bank that will eventually hold 200 iPS cell lines. Standardizing the protocol for banking iPS cell lines is a labour-intensive process requiring analysis of cell morphology, cell surface antigens and gene expression profiles, and monitoring for unexpected changes. "We need to be able to grow the cells in a strictly defined medium so that we can differentiate them stably and with a high level of reproducibility," says Miho Furue-Kusuda, who is in charge of the bank. Analyses using the cells will benefit from NIBIO's toxicogenomics database, the largest in the world, which collects data on the effects of more than 150 drugs in rats.

Standardized protocols for producing iPS-derived cells will be the foundation for new guidelines on their use in pharmacological testing. Mizuguchi hopes to have the protocols in place within two years. "Japan is the only country moving forward so quickly towards the use of iPS cells to validate new drugs," says Mizuguchi.

Bioresources research

NIBIO is developing other resources that will give a crucial boost to pharmaceutical studies.

For example, NIBIO's DNA bank has started to make available quality-controlled resources derived from patients suffering from 130 rare diseases. The bank distributes cDNA clones from chimpanzee and crab-eating macaques along with related genetic sequences.

A unique experimental mouse has also been established at NIBIO. Whereas conventional

severe combined immunodeficiency (SCID) mice can only hold transplanted human tissue for a few weeks, NIBIO's 'Super-SCID' mice maintain human tissue transplants, such as lung, thyroid and skin, for a year or more, a boon for drug development and the study of environmental hazards. In addition, NIBIO holds mice that develop various diseases spontaneously. "We can watch the natural development of chronic diseases rather than making artificial disturbances with mutagenesis or transgenes," says NIBIO's Tohru Masui.

The resource bank also includes a cell bank of cultures of human brain, lung, liver, kidney, gut and blood cells, as well as many samples of mesenchymal stem cells and cells derived from patients, which are important for drug development and regenerative medicine. Through extensive quality control and monitoring, NIBIO ensures that there is no contamination by microorganisms or other cell types. This is not easy considering a recent study by NIBIO's Arihiro Kohara showing that 26% of cell cultures in Japan contain mycoplasma. "These figures are similar to those seen all over the world," says Masui. "It shows the importance of quality control. Contamination has a huge impact on the reliability and repeatability of experiments."

Research Center for Medicinal Plant Resources and Tsukuba Primate Research Center

The vital experimental resources available through NIBIO also include primate and medicinal plant collections.

The Research Center for Medicinal Plant Resources has four bases across the Japanese archipelago, representing different climatic areas.

New restrictions on crude drug exports in China as well as quality-control problems prompted the cultivation of several important medicinal plants locally. The centre cultivates and preserves over 4,000 plant species to supply seeds and seedlings, and offers guidance on cultivation technology to research institutes. "It's the most comprehensive collection in Japan," says Yamanishi.

The Tsukuba Primate Research Center, with 2,000 cynomolgus macaques, also offers a unique resource. The monkeys are mated in specifically selected pairs so that hereditary factors can be traced. The centre carries data on the monkeys' age, laboratory test results and family histories stretching back 30 years, enabling researchers to predict, for example, which monkeys might experience high blood pressure. "We know the entire history of these monkeys," Yamanishi says.

The monkeys, used at NIBIO for vaccine and other research, are also available to scientists and pharmaceutical companies throughout Japan for research on disorders such as hereditary diseases, diabetes and cardiovascular disease.

Yamanishi hopes that these resources, maintained at high levels of quality, and the research that NIBIO supports will give the pharmaceutical industry a push. "These kinds of research and resources are essential for drug development, but neither the universities nor the drug companies are doing it. We've only been around for four years, but we're already starting to see results."

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