NEWS IN BRIEF

Cancer mouse models carry genomic inconsistencies

Preclinical disease models are always flawed. In the case of patient-derived xenograft (PDX) mouse models of human cancer, a new study in *Nature Genetics* has catalogued some of the ways in which these 'avatars' lead scientists astray.

PDX models of cancer — in which cancer cells are harvested from patients and injected into mice — have become increasingly important in cancer research. Not only do researchers think that these *in vivo* models of cancer are more representative of human disease than *in vitro* cell line approximations, but they also offer the promise of enabling an empirical approach to precision medicine. By taking cells from a patient and building a personalized mouse avatar, researchers can, in theory, test targeted drugs and chemotherapies on an individualized basis before choosing a best option.

Given the growing importance of these models, cancer geneticist Todd Golub, at the Broad Institute in Massachusetts, and colleagues set out to study how well PDX mice mimic human disease. They assessed over 1,100 models, and found considerable genomic and phenotypic differences in terms of the evolution of PDX and human cancers. PDXs rapidly picked up copy number alterations as they were passaged, which led to different genomic architectures from those of the originating tumours. "The assumption is that what grows out in the PDX is reflective of the bulk of the tumour in the patient," Golub told *Nature News*. "But there's quite dramatic resculpting of the tumour genome." These changes may influence how PDXs respond to chemotherapy and targeted drugs, he cautions, raising new considerations for researchers that rely on these models.

Nevertheless, some groups hope that new approaches to PDX-model generation — including the use of mice that have been genetically engineered to carry human genes — could make these models less flawed.

Asher Mullard

$215 million cancer immunotherapy biomarker consortium debuts

The NIH and 11 biopharmaceutical companies have partnered to identify, develop and validate new biomarkers that will accelerate the development of cancer immunotherapies.

Because these drugs recruit the immune system to kill tumours, conventional criteria for measuring responses to cancer therapies may not effectively capture therapeutic activity. Drug developers therefore need a whole new set of tools to identify patients who are likely to respond, track the emergence of resistance, understand how the drugs act and monitor success in clinical trials (*Nat. Rev. Drug Discov.* **15**, 807–809; 2016). Over the next 5 years, the US$215 million Partnership for Accelerating Cancer Therapies (PACT) consortium will work precompetitively to find biomarkers that can help address these issues. Although companies have been searching for biomarkers on their own, by working together they can pool resources and expertise, while also ensuring that data are uniform, harmonized and comparable across different trials.

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PACT's industry partners consist of AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Genentech, Gilead Sciences, GlaxoSmithKline, Janssen, Novartis and Pfizer. Each partner will contribute up to $1 million per year, and the NIH will contribute the remaining $160 million. PACT will be managed by the Foundation for the NIH (FNIH). The FDA is serving in an advisory role.

Asher Mullard

FDA unveils searchable adverse events system

The FDA has launched a new adverse event portal that enables drug developers, doctors and patients to search for safety red flags for approved drugs. This FDA Adverse Event Reporting System (FAERS) could offer a powerful post-marketing pharmacovigilance resource and a means of guiding preclinical drug development.

Prior to the unveiling of the new system, researchers had to download FAERS data sets and develop their own programmes to analyse the inputs. With the updated system, they can query the database online to generate reports for specific products and adverse events, over different time frames. The agency hopes that the increased transparency of the new system will spur stakeholders to submit more detailed and complete reports, increasing FAERS's utility further.

However, a team of academic and industry researchers cautioned earlier this year in *eLife* that the FAERS database is riddled with data problems. Due to the lack of data curation and standardization, for example, each drug has on average 16 different names in the system. The antidepressant fluoxetine had 378 synonyms. The descriptions of different adverse events also varied widely, and side effects tend to be reported more often when drugs are in the news, introducing a potential source of bias.

Nevertheless, the researchers concluded that with curation, FAERS offers an invaluable data set — even for preclinical drug discovery programmes. The same team of researchers showed in *Nature* in 2012 how computational analyses of drug structures could be used to discover novel toxicity liabilities for approved drugs. By comparing the chemical structures of novel candidates with those of approved drugs, and by feeding curated data from FAERS into this analysis, researchers may be able to discover possible toxicity red flags and mitigation strategies for preclinical candidates.

Asher Mullard