Orienting cancer

By Steve Edelson, Executive Editor

Eli Lilly and Co., Merck & Co. Inc. and Pfizer Inc. have joined in a precompetitive deal to study the pharmacogenomics of Asian cancer patients. By jointly gathering molecular epidemiology information on a large scale, they expect to optimize the return on investment for all three players, although the ensuing drug discovery and development will remain within the competitive space of each company.

Under the February partnership, the companies formed the not-for-profit Asian Cancer Research Group Inc. (ACRG), a virtual entity tasked with building a pharmacogenomic cancer database of about 2,000 tissue samples from the most common cancers in Asia. The Lilly Singapore Centre for Drug Discovery will provide the infrastructure to house and oversee the resulting open-source database.

ACRG first will focus on gastric and lung cancers.

"There's great evidence that cancers are different in Asia than in other parts of the world," said Kerry Blanchard, VP and leader of drug development in China at Lilly.

For example, in Asia and elsewhere, one of the best-documented examples of genetic variation among cancer patients are the multiple variants of *epidermal growth factor receptor* (EGFR), a target hit by many small molecules and antibodies.

In China, a specific mutation in EGFR is present in 40%–60% of lung cancer patients compared with in only 3%–5% of patients in the U.S.¹ Response rates to EGFR inhibitors are different in patients with this mutation, and therefore personalizing treatment is a challenge.

"The pharma industry's and Eli Lilly's view in general is that patient tailoring is important. We thus need a great amount of information to accomplish this," Blanchard told *SciBX*.

Enter ACRG, the idea for which came out of discussions between Blanchard and Stephen Friend, who was VP of oncology at Merck and CSO of its Rosetta unit. The pharma shuttered Rosetta last year, and Friend, along with former Rosetta executive scientific director Eric Schadt, relaunched the operation as a not-for-profit institute called **Sage Bionetworks**.²

"Friend and I have known each other for quite a long time, and in thinking about the need for specific patient-tailoring in Asia, we decided to focus on noncompetitive work," said Blanchard. "Steve and I both had relationships with Neil Gibson at Pfizer and talked to him as well."

Gibson is CSO of Pfizer's oncology research unit.

During the discussions about forming ACRG, Blanchard told *SciBX* there was "no haggling over what would be precompetitive. First you define the areas in which you do compete—we all compete in the process of actually making drugs. The generation of this type of almost molecular epidemiology data is really not competitive. It will take these data combined with many types of data—some internal, some external—to move into a competitive sphere. We really compete on finding and making the molecules."

"There was never any discussion I was involved with other than 'generate data and get it into the precompetitive landscape,'" said Gary Gilliland, franchise head of oncology and SVP at Merck's Merck Research Laboratories. "This is expensive and suited to what pharma can do."

Strength in numbers

Although the ACRG model could be applied to other disease areas, Gilliland thinks cancer is an ideal starting point. "Genomewide association studies show there are lots of modest effects in common diseases, but in oncology there are alleles that are clear disease drivers," he said. "Cancer is in the forefront because it's absolutely essential to understand the genetics to predict response."

However, Gilliland noted, to find the causal alleles in cancer, "you need thousands of samples because there are so many mutations in a cancer and because the best way to validate a mutation is to show it recurs. By pooling resources from

three companies we can manage this. We triple the power at a third of the cost to each company."

"For molecular epidemiology studies in complex syndromes like cancer, the size of the sample set that you need to have stat power is quite large," said Blanchard. "As you start filling out the things you'd like to do on the number of samples you'd like to have, it becomes a very big project. It's certainly more than hundreds" of samples.

Deep analysis

Even though ACRG will collect the tissue samples and generate the corresponding pharmacogenomic profiles, any analysis of the data will be carried out elsewhere—under the roof of Lilly, Pfizer or Merck, or any other entity that wants to access the sample database.

"Every company will approach the analysis slightly differently," said Gilliland. "The dataset is useful because we're planning clinical annotations such as poor prognosis. We'll use the data to test and validate new mutations that might be drivers for tumors and to find biomarkers of response."

Internally, he said, Merck plans to take the dataset and "bring it back into somewhat more practical preclinical mechanisms for drug discovery. We'll look at cell lines with some reasonable resemblance to the primary tumors."

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—Kerry Blanchard, Eli Lilly and Co.

“The intent of ACRG is to put together the research plans, collect samples and publicly host them,” added Blanchard. “The individual companies will have access to the data just like everyone else. I don’t expect that the ACRG entity will be studying the data and doing deep analyses. Each of the companies will do that independently.”

Blanchard expects it will take about 2 years to collect and process the 2,000 samples. In addition, ACRG hopes to collect three years’ worth of outcomes for each sample. “You can’t collect 2,000 samples at the exact same time. Analyses will be done in batches and data will come out in batches,” he said.

As ACRG’s data emerge, a likely outcome will be comparing and potentially merging the Asian database with those from groups in the U.S. and EU that are collecting deep data on cancer patients. These groups include the Cancer Genome Atlas, which is a joint effort between

the NIH’s **National Cancer Institute** and its **National Human Genome Research Institute**.

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COMPANIES AND INSTITUTIONS MENTIONED

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