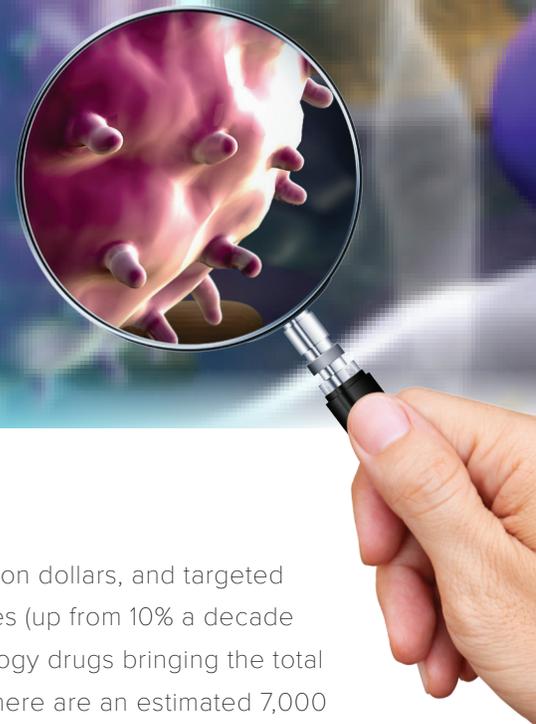# Systems Imagination

Old Drug New Purpose

A Case Study in Leveraging a Multiscalar Systems Medicine Approach for Oncology Drug Repositioning

Introduction

Apply big data to discover drug repositioning insights

Global oncology spending will soon be over $100 billion dollars, and targeted drugs now make up nearly 50% of cancer-related sales (up from 10% a decade ago). In 2015 alone, the FDA approved 45 new oncology drugs bringing the total number of approved oncology drugs to about 200. There are an estimated 7,000 cancer therapies in development worldwide, many at universities and small private biopharma groups. There is also an unprecedented growth in publically available big data, especially from cancer genome projects, making it possible to leverage molecular intelligence to rescue and reposition many of the cancer therapies that have failed to advance through clinical drug development. However, there are important barriers making it difficult to apply big data to discover drug repositioning insights that can help rescue drugs with potential to help cancer patients.

Client Need

Discover insights to maximize drug potential

The client was interested in applying a systems modeling approach to mine the publically available cancer patient profiling data, in order to discover novel insights that could be used to invest in acquiring and rescuing some of the thousands of cancer drugs that have failed to advance through clinical drug development. The underlying thesis is that some of the cancer treatments were either not properly positioned to the right indications and/or they did not leverage the right drug combinations to achieve the expected patient benefits, and a systems modeling approach could solve those issues. The SII evaluated the clients needs, and identified a number of resource and modeling challenges that needed to be solved.

The Challenge

Aggregation of disparate and difficult to access sources of information

The first challenge is that there is no centralized, organized, and comprehensive resource cataloging these efforts. Many promising therapies are available for licensing through individual university technology transfer offices, but finding and searching these websites for mechanistic information about the available drugs is time-consuming and cost prohibitive. The second challenge is that molecular and clinical data from deep patient profiling is also difficult to access. Although efforts like The Cancer Genome Atlas project represent a valuable resource to the research community, accessing and curating the data and fusing it with prior knowledge is a formidable challenge. Finally, even with the aggregation and amalgamation of drug profiling and disease profiling data, mapping mechanistic insights from various diseases to different drug mechanisms to multiple disease contexts represents both a computational and modeling challenge that most groups have not been able to effectively solve.

The Novel Approach

Repurpose older drugs and identify new therapies

The collaboration between SII and the client evolved to a strategy that involved both a bottom up and a top down approach to discovering novel drug repositioning insights. In the top down approach, the SII clinical oncology advisory team identified a set of important oncologic targets and pathways where no approved therapies currently exist. Using this approach, SII analyzed associated and interacting pathways to identify key targets, then searched for appropriate patents and publications seeking drugs developed for other therapeutic areas. The approach was to re-purpose older drugs and identify new therapies that could be available for licensing for further development in oncology.

In the bottom up approach, a comprehensive knowledge base was created to integrate TCGA data and link it to prior knowledge and comprehensive data from a large catalogue of available drug candidates, which was then used to support advanced systems modeling to identify insights that might be beyond human imagination. This modeling approach was then coupled with the top down approach to deliver a truly differentiating opportunity to the client.

Value Added

Rapid identification of new innovative therapies

We identified new, innovative therapies being developed that published promising pre-clinical or Phase I results with an opportunity to license. Within 90 days, SII presented the client with solid leads that are patented or patent-pending and available for licensing. To date, SII has delivered solid leads to the client, and continuing to discover unknown knowledge that could be leveraged to rescue drugs with potential to improve the lives of patients with multiple types of cancer.