1. **Title:** Methods for identifying drug targets based on genomic sequence data **Date of filing:** Dec 13, 2013 **Date of publication:** Apr 23, 2015 **Design Classification:** G06F19/12, G06F19/18 **Summary:** The invention provides a computational approach to identifying potential drug targets, specifically antibacterial drugs, by annotating genome sequences. The method starts by locating open reading frames and assigning a metabolic genotype based on the sequences. The assigned metabolic genotype corresponds to a stoichiometric matrix, as part of the patent, and the matrix is subsequently used to assess flux balance analysis of antibacterial drugs simulated as genetic deletions. **Patent relationship:** The antibacterial simulation strategy using flux balance analysis echoes our simulation of cancer therapeutics using constraint based analysis. It would be useful to observe how the patent incorporates genomic analysis to simulating drug targets. **Limitations:** The patent limits our innovation space by protecting the workflow in constructing genotype-specific metabolic stoichiometries. If this patent did not exist, we could pursue the construction of genotype-specific biomass stoichiometries as opposed to using a central and shared human metabolism stoichiometry.

**2. Title:** Computer-based system, methods and graphical interface for information storage, modeling and stimulation of complex systems **Date of filing:** Jan 17, 1995 **Date of publication:** Nov 9, 1999 **Design Classification:** G06F19/18 **Summary:** This invention provides an integrated computer-based graphical interface for visualizing dynamic models simulating complex systems. Specifically, the patent describes the visualization of chemical processes which are connected by interactive arrows and boxes. These arrows and boxes can be used to build interactive network pathways in which quantitative values can be assigned to each reaction. **Patent relationship:** The way we visualize our simulation results is also by mapping our flux solutions onto a complex yet visual metabolic map, depicted in the same manner described. Without such a visualization tool, it would be hard to understand the scope of our simulations just by looking at numbers. **Limitations:** This patent limits our innovation space by delineating a specific way of representing complex systems comprising of building blocks and reactions, and we have to be wary our graphical representation does not overlap theirs. If this patent did not exist, we would have more flexibility in choosing how to visually represent our metabolic map.

**3. Title:** Methods and systems for genome-scale kinetic modeling **Date of filing:** Feb 19, 2008 **Date of publication:** Jan 13, 2011**Design Classification:** G06F19/12**Summary:** This invention provides a method for developing data-driven dynamic models of biological networks. In particular, it covers the grounds of the construction, analysis, and characterization of dynamical states of networks at the cellular level. These are achieved by constructing matrices from high throughout fluxomic, metabolomic, and proteomic data. **Patent relationship:** This invention provides the know-how that our design utilizes in setting up our project’s constrains for constraint-based and kinetic analysis. Without these constraints and kinetic parameters, we would not be able to observe perturbations in our metabolic model. **Limitations:** This patent would limit our project’s ability to execute any of our computational modeling on cancer metabolism using our current workflow. Because the inventor of this patent is Dr. Palsson, our advisor, we have capitalized on this novel invention and enabled us to analyze cancer metabolism mechanistically.

**4. Title:** Method for the evolutionary design of biochemical reaction networks **Date of filing:** Aug 27, 2001 **Date of publication:** Oct 24, 2006 **Design Classification:** G06F19/12 **Summary:** This invention relates to methods for achieving an optimal function of a biochemical reaction network. The methods described encompass the in silico construction of biochemical networks, and laboratory methods to confirm in silico results. To summarize, this patent covers the grounds for using in silico methods to optimize biochemical production and experimental methods to confirm it. **Patent relationship:** The invention describes a workflow in which experimental methods can be used to complement and confirm in silico methods. We can learn from this invention to design experiments to verify the project’s in silico simulations.  **Limitations:** This patent would limit our project’s innovation space by eliminating several cell culture procedures to experimentally verify the project’s in silico results. Again, because the inventor of this patent is Dr. Palsson, we are able to use these methods under his realm.

**5. Title:** Pharmacogenomics and identification of drug targets by reconstruction of signal transduction pathways based on sequences of accessible regions **Date of filing:** Apr 27, 2001 **Date of publication:** Aug 26, 2003 **Design Classification:** G06F19/22 **Summary:** The invention describes methods in identifying drug targets using pharmacogenomics and the reconstruction of signal transduction pathways. In particular, the methods are used to suggest gene therapy and suggest regulatory sequences that drug targets can bind to. In addition, the methods described can assess potential pharmacological side effects of regulatory sequence targeted drugs. **Patent relationship:** This patent relates to our project in that it delineates methods to predict drug response to certain therapeutics. This in particular aligns with our project in that they analyze drug responses to particular genotypes, much like how we plan on assessing drug responses to particular enzyme mutations. **Limitations:** This limits our innovation space by focusing on drugs that target metabolic pathways, whereas this patent covers the grounds for therapeutics targeting signal transduction. If this patent were lifted, we would be able to explore therapeutics that target regulatory pathways and not be limited to cellular metabolism.

**6. Title:** Method for determining gene knockout strategies **Date of filing:** July 9, 2003 **Date of publication:** March 4, 2004 **Design Classification:** G06F19/12 **Summary:** This invention describes a bioinformatics approach to model gene deletions from a metabolic network by selecting a cellular objective for an organism and optimizing around it. **Patent relationship:** The method described is similar to the constraint-based approach our project utilizes in analyzing perturbations. This invention is useful for us in that it optimizes certain organism objectives as we can use this to maximize our objectives around tumor growth. **Limitations:** This patent limits our invention space in using certain methods to mimic gene knockouts in the models. If this patent were lifted, we would be able to use a more efficient algorithm for objective optimization.

Many of the patents our team found regarding biological computational modeling were invented by Dr. Palsson, and this is evident because all of the analytical methods we use from metabolic mapping, constraint-based analysis, and kinetic analysis are proprietary software developed by Dr Palsson’s lab. Searching through the patents have inspired a deeper appreciation in Dr. Palsson’s efforts in developing foundational approaches to computational modeling. As a result, we have opted to restrict our use of software to the plethora of proprietary material under Dr. Palsson. Thus, as long as the research is done under Dr. Palsson’s lab, which still gives us a lot of flexibility, we will be free of patent infringement regarding metabolic modeling.

I learned the value of research in fundamental fields, such as developing the math for modeling purposes, that I never understood before through this patent search as they serve the solid foundation of present engineering approaches. I also learned that many computational approaches can be patented that is not limited to software. Methodologies and workflows are viable for being patented as well. Moreover, these workflows can also be patented in their application to specific purposes, for example, transduction pathways. Thus, these lessons have inspired us to place a strong emphasis on the development of our workflow in addition to the discovery aspect of oncogenic metabolic relationships and we look forward to preparing a manuscript regarding a proof of concept of this workflow.

**REFERENCES:** [1] InterTech Ventures Ltd,. Computer-based system, methods and graphical interface for information storage, modeling and stimulation of complex systems. (1999). [2] The Regents Of The University Of California,. Methods for identifying drug targets based on genomic sequence data. (2015). [3] University of California, San Diego,. Methods and systems for genome-scale kinetic modeling. (2011). [4] University of California, San Diego,. Method for the evolutionary design of biochemical reaction networks. (2015). [5] Sangamo Biosciences Inc,. Pharmacogenomics and identification of drug targets by reconstruction of signal transduction pathways based on sequences of accessible regions. (2003). [6] Penn State Res Found,. Method for determining gene knockout strategies. (2015).