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To whom it may concern:

I am pleased to write a letter on behalf of Tulio Torezan Silingardi Del Claro who I hosted in my lab as a summer intern from May 25, 2016 until August 12, 2016. It was a great pleasure working with Tulio, who made significant progress in the short 11 weeks that he was with us. He shows every sign of maturing into a promising young scientist. Below I outline the work he accomplished and speak to the qualities in his abilities that I was able to witness during this time.

My lab develops methods to integrate genetic pathway information for the analysis of cancer genomics datasets. We are interested in predicting and improving cancer outcomes. Our methods infer activity levels for all of the genes in a pathway model given gene expression, copy number, methylation, and proteomics level data. In addition, we develop machine-learning classifiers to predict drug response that are guided by pathway information.

We have been struggling with the problem of how to then use these results to come up with actionable clues for individual patients. While we have demonstrated that the network models contain relevant genes and their interactions, we have lacked a principled approach for determining which particular genes might be good targets for therapy. This is where Tulio's project came in.

Tulio came up with an elegant approach that uses "network flow" on a pathway model to address this issue. The intuition is that important genes involved in the tumor biology are those that communicate with many other genes in the implicated network. Network flow quantifies this idea by connecting the genetic network with introduced "sources and sinks" and allowing fluid to flow through pipes that connect the genes together based on their known signaling. Tulio came up with a strategy to convert a patient's data, provided as lists of genes that are mutated or activated/inactivated, into capacities on the pipes in the flow network. He also wrote, from the ground up, the Ford-Fulkerson algorithm to implement the network flow. Tulio also then developed his own novel approach that we call Network Disruption Analysis (NDA) that considers deleting each gene out of the network, along with its associated pipes, and then measuring the amount of flow that is limited in this situation. The amount of flow reduction is used as a quantification for our disruptive to the signaling each gene's deletion is associated with. Tulio showed that ranking genes based on his NDA score significantly enriches for genes known to be involved in the cancer process. He demonstrated this on a breast cancer network that was able to recapitulate most of the known drivers in luminal versus basal breast cancers. This result was outstanding and far exceeded my expectations for the project.

Based on Tulio's success, we are now re-configuring our patient-specific network analyses and will work toward testing them in cell line models with our colleagues at Harvard. Should these prove successful, we will write a paper describing this work. Tulio will certainly be included as a contributing author for his major contributions to this development. It is a rare honor for a summer intern to have such a successful project that it merits inclusion into a manuscript and invitation of the student as a co-author! This really proves Tulio is functioning at the level of a mid- to senior-level graduate student.

He independently moved this project forward, gave clear presentations at our individual and group meetings, and was able to solve challenges as he encountered them in a very efficient manner.

In summary, Tulio had one of the most successful summer rotations in my lab among all students that have worked with me. I was truly impressed with what he was able to do in the little time that he had. He was very pleasant to interact with, was extremely intelligent, had great programming skills, and communicated with me and the rest of the lab very effectively. I do hope he decides to continue pursuing a scientific career. I see a lot of promising opportunities for him in the future. Happy to answer any questions you might have.

All the best,

A handwritten signature in black ink, appearing to read 'JMS', with a stylized flourish at the end.

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