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BIFX-545

Discussion Questions Week 3

2/16/2022

1. Write a very generalized 4-5 sentence summary of "Genomic Signatures to Guide the Use of Therapeutics" that explains what they were trying to achieve and what they found.

Advances in chemotherapeutic agents have helped us combat cancer, however individuals are not always receptive to the same drugs. There has been a lack of predictive tools to determine which drugs would be best for the individual. This study uses microarray data and gene expression signatures to create models that predict clinical and therapeutic responses to certain drugs or multidrug regimens. The results could help us better use these drugs.

1. Write a very generalized 4-5 sentence summary of "Primary Prevention of Cardiovascular Disease with a Mediterranean Diet"

Previous research had indicated that there might be a negative association between a Mediterranean diet and cardiovascular risk. This study set out to explore this more directly by setting high cardiovascular risk participants on different diets and measuring their rate of major cardiovascular events. In the end, the researchers concluded that participants the Mediterranean diet had less cardiovascular events.

1. Pick one of these two papers to read more critically. We will be looking more deeply into the "Genomic Signatures..." paper in future weeks, so that paper is preferred, however, that paper contains a lot of bioinformatics techniques that are likely to be unfamiliar to most of you. Therefore, it is perfectly fine if you choose to critique the "Mediterranean Diet" paper instead. Using whichever of the two papers that you choose, please answer the following questions:
2. What are the main questions that are addressed in the manuscript?

Could genomic predictors of chemotherapy sensitivity be found? Could models be developed to use such predictors in determining which cytotoxic agents were most likely to respond? Could models be used to predict multidrug regimens, rather than just single ones?

1. Are the experiments that are described in the paper sufficient to completely answer each question? If not, why not?

They built a model to predict docetaxel sensitivity by examining resistant and sensitive cells and genes. This allowed them to predict both sensitivity and response. This was compared to clinical studies to verify it. Their model correctly predicted docetaxel response in 22 of 24 clinical samples with an accuracy of 91.6%. Similar results were found in other drug types. The procedure seems solid, since they compared their predictions to real data. However, the limited number of data sets is concerning.

1. Assuming the original samples or raw data were available to repeat the experiments, could someone who knows how to do the basic techniques that were used (i.e. how to do a western blot etc.) replicate the results that are presented in the paper based on the methods that were provided? Why or why not?

The original article does not have the full methods and simply provides a brief overview. It talks about what programs were used and how to treat the data, but doesn’t go into much detail on how all the figures were generated. With the article alone, it would seem difficult to replicate their results. However, it provides a location at which the “complete” methods may be available. This could provide the necessary details.

1. What information (if any) is missing from the materials and methods section? Are there any results that come from an experiment or method that was not described? Is sufficient detail given to allow the experiments to be repeated?

As hinted in the previous answer, there is doesn’t not appear to be enough information in the article alone to replicate the experiment. The general procedures are outlined, as well as how the data was treated. However, there seems to be little to no information about how the different figured were generated and with which settings. This seems like a critical piece of missing or lacking information, given how many figured were used. But the supplementary materials may have more details than the article itself.

1. What information (if any) is missing from the results section? Is a result given for each experiment that was described?

The results section is kind of confusing, because it is split up based on all the different models they made. There was an initial predictive model that worked with docetaxel. Then they applied these techniques to other drugs. Then they used it to predict response from multidrug regimens rather than single drugs. Finally, they use it to predict chemotherapy responses across tumor types and linked chemotherapy sensitivity to oncogenic pathway status. Ultimately, each section did explain the models that were made, and the degree of success they achieved.

1. Are the results that are presented sufficient to support the conclusions that were made?

Their models were constructed from real cell and gene data. They confirmed their accuracy against clinical trials. It looks promising and I think it is fair to concluded that such techniques could be potentially used to help better tailor treatment options to the individual.

1. Are there any conclusions or discussion points that seem like overstatements given the results that are presented in the paper?

I think the authors are on the right track with their work. However, their study alone doesn’t seem to have a large enough sample size to draw any definitive conclusions. Assuming that those handful of clinical studies (Approximately 20 to 30 per drug) each represented single individuals, there has not been enough research done to apply these results to the wider population. More studies should be done with these models.

1. Should the manuscript be published in its current form? If not, what needs to be done before it would be ready for publication?

The manuscript as a whole seems alright. The beginning is a little confusing, since the introduction wasn’t labeled. But the figures all seem to be of a proper size and adequately labeled. The purpose of their research was clearly stated, along with all their results. The methods could be more clearly explained, unless the supplemental materials are sufficient.

1. Is there anything in this manuscript that should have stood out to a competent reviewer as a potential warning-flag that the data, methods, results, or conclusions might be unreliable?

The small clinical sample size definitely stood out to me, but the article was published in Nature so perhaps I am misunderstanding how that works.