Re: U01 *“Evaluating the functional impact of coding and non-coding somatic*

*mutations over multiple scales”*

June 10, 2017

Dear Mark and Haiyuan,

I am most happy to write this letter of support as Director of the Department for Biomedical Research at the University of Bern (Switzerland) and PI of the NCI Prostate Cancer Specialized Programs of Research Excellence (SPORE) at Cornell. As you are aware, my laboratory moved this past May to Bern but I maintain 30% effort at Weill Cornell Medicine in New York to co-lead the Cornell SPORE in prostate cancer. We have established MTAs in both direction to ensure a simple flow of materials and reagents that were developed at either site for prostate cancer research. For example, I developed a robust organoid program in New York (Pauli et al., Cancer Discovery 2017). We have established a similar activity in Bern and now have access to over 10 human benign organoids. We anticipate that for this U01 application we will continue to develop these organoids.

As the developer of the WCM SPORE, over the past 10 years we have accumulated highly valuable genomic and transcriptomic data from a number of sources that may help with this project. For example, I am one of the PIs for the SU2C/PCF Castration Resistant Prostate Cancer (CRPC) 500 study (Robinson et al., Cell 2015 and Pritchard et al., NEJM 2016). We are currently finalizing the genomic and transcriptomic data for over 500 CRPC cases with complete pathology and clinical outcomes data (including treatment). Given a focus on TP53 and RB1 in this study, this and out Neuroendocrine Prostate Cancer (NEPC) cohort will be highly valuable. As we recently reported in Beltran et al. (Nature Medicine 2016), advanced CRPC but particularly NEPC have TP53 and RB1 genomic alterations. This is highly relevant for one area of translational focus for our U01 proposal.

We look forward to extend our many year collaboration with the Yale and Cornell groups.

Best regards,

MAR