

Wednesday 17th October 2018

Dear Brandon,

Here is a letter of support for your internal *Critical Path* funding proposal titled, "High-throughput truthing of microscope slides to validate artificial intelligence algorithms analyzing digital scans of same slides: data (images + annotations) as an MDDT." I am enthusiastic about your plans to create regulatory grade annotation data (medical device development tool), and I am willing to participate and recruit readers from the consortium I lead (www.tilsinbreastcancer.org).

The evaluation of tumor infiltrating lymphocytes appears very promising for prognosing cancer, and the pathologist community needs training in this area. I chair a consortium of mainly expert-pathologists that was installed in 2014 and includes mainly pathologists with expertise and interest in the immuno-oncology biomarker area, including expert clinicians and statisticians. For a full member list, please consult www.tilsinbreastcancer.org. See also <https://www.tilsinbreastcancer.org/researcher-resources/> for a recent Special Issue in *Seminars in Cancer Biology*, Impact Factor 10.198) this group has developed on Immuno-Oncological Biomarkers. You co-developed one of those papers on machine learning and TIL-evaluation (<https://www.sciencedirect.com/science/article/pii/S1044579X1830066X>).

The group has evolved to having >100 pathologists on board, from about 40 different laboratories in the US, EU, Asia and South-America, including the expert-pathologists from the Biomarker Groups of Merck, Roche-Genentech, Astra Zeneca, all having expertise on TIL-assessment. We do not ask for funding from the participating companies to avoid conflicts of interest. The continuous inclusion of experienced pathologists, assisted by expert clinicians like Sherene Loi, Sylvia Adams and Sybille Loibl, and expert statisticians like Stefan Michiels make the Working Group the leading expert group on TIL-assessment worldwide.

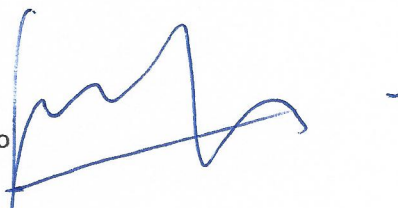
Relevant for the submission of this proposal, the Working Group, with your input has developed a manuscript entitled "Scoring of tumor-infiltrating lymphocytes: from manual estimation to machine learning", Klauschen et al. *Seminars in Cancer Biology* (Impact Factor 10.198). This is a perspective paper on TIL-assessment by machine learning methods and serves as the basis for this grant submission.

If I can, I will also use my network to introduce you to leadership people in pathologist societies and associations. I agree with you that these are excellent opportunities to get pathologists to participate in the studies FDA is conducting on quality assurance of machine learning applications in pathology. On a related note, I would like to invite you to speak at our meeting Dec. 6, which is attached to the San Antonio Breast Cancer Symposium. It will be a great opportunity to share the project, develop the data-collection protocol, and possibly collect some data!

I wish you success with your funding application and your aims and objectives. I think you are doing a great job leading the communities of pathologists, hardware manufacturers, and algorithm developers towards methods and tools that will have a positive impact on public health.

Sincerely,

Roberto Salgado

A handwritten signature in blue ink, appearing to read 'Roberto Salgado', written over a horizontal line.