AI-driven image-based microbiome analysis reveals correlation of higher pre-treatment microbiome level with complete response in QUILT 3032 trial patients

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The human microbiome, both systemic and tumor microenvironment (TME)-associated, exerts a profound influence on cancer development, progression, and response to treatment. To facilitate microbiome analysis in cancer, we developed an AI-driven computational pathology system that determines relative microbiome levels in H&E-stained slides from formalin-fixed paraffin-embedded tissue specimens.

We utilized available whole-genome and whole-transcriptome sequencing data for microbiome detection in TCGA bladder cancer [Poore et al. 2020; Nature 579], for which images were available, to define microbiome-low and -high labels. The TCGA bladder cancer cohort (n = 408) was distributed into training (66.7%, n = 272), validation (8.3%, n = 34) and test (25.0%, n = 102) sets; each with equal numbers of microbiome-low and -high patients. The cohort featured an average of 1.05 diagnostic (DX) images per patient, with 429 DX images in total.

We trained a deep network using a total of 303,104 patches (of size 100 x 100 microns, equivalent to 400 x 400 pixels at 40X magnification) randomly selected from 296 DX images in the training set. Testing on untouched patient data (n = 102) gave area under the ROC curve of 0.74 and F1 score of 0.74.

The developed system was then used to determine correlations between TCGA bladder cancer patient survival and microbiome level. Treatment-naïve bladder cancer patients identified as microbiome-low by our image-based system had higher survival rates, with hazard ratio of 1.45.

Further, we assessed correlations between pathologic complete response (pCR) at 12 or 27 weeks and microbiome level in non-muscle invasive bladder cancer patients in ImmunityBio, Inc.’s QUILT-3.032 trial. Patients that achieved a pCR with treatment were found to have significantly higher probability of microbiome-high pre-treatment, as compared to those who did not achieve a pCR. Reductions in predicted microbiome levels after treatment were also observed in pCR patients. Conversely, 6 of 7 non-responders were found to have an increase in microbiome-high probability with treatment.

These findings suggest our novel AI-driven image-based computational pathology system has the potential to provide data that may not only inform clinical decision-making, but also allow further investigation into the role of the TME microbiome in cancer.