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803.EMERGING TOOLS, TECHNIQUES AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

Artificial Intelligence of the 2-D and 3-D Bone Marrow Microenvironment to Identify Cytogenetic Subtypes of Multiple Myeloma

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Multiple myeloma is the second most common hematologic malignancy with an annual incidence of 35,000 new cases every year in the U.S. Due to improved access to effective therapies, overall survival has improved from 1-3 years to over 10-20 years. However, there is not yet any available curative therapy for multiple myeloma and most patients will suffer from recurrent relapses, with an unmet clinical need for novel therapies. The interplay between the bone marrow microenvironment and malignant plasma cells is critically important to better understand pathogenesis of the disease, to predict response to therapy (in particular, immunotherapy), and to identify novel drug targets. Leveraging the power of computer vision, we are developing novel machine learning algorithms to label and characterize individual cells from digitalized H&E and CD138 stained plasma cells in bone marrow core biopsies. A total of 188 patients were included in this analysis: 157 with multiple myeloma, 6 with monoclonal gammopathy of undetermined significance, 17 with smoldering multiple myeloma, and 6 with primary amyloidosis. The deep learning framework to build our artificial intelligence (AI) models is implemented by Pytorch. Using the surface creation tool from the Imaris 10.0.1 software, we are able to measure pixel intensity, area, sphericity, and other cellular features that are then correlated with myeloma clinical outcomes as well as defined cytogenetic subtypes of multiple myeloma in 2-D. As a preliminary step in this project we analyzed the IMARIS software's ability to accurately determine the number of plasma cells compared with clinical standards through a linear regression plot with strong correlation (R^2=0.9). In addition, we rendered the 3-D microenvironment by combining more than 60 sequential formalin-fixed paraffin embedded (FFPE) tissue block bone marrow biopsy samples sliced at a thickness of 4 microns. Through utilizing the surface creation tool on the 2-D images within the 3-D model, we can show distance measurements between plasma cells and other features of the microenvironment such as adipocytes. This insight allows us to better understand and control the immune microenvironment through observing the various 2-D tissue slices within the 3-D model. Furthermore, we have assessed whether multiple myeloma digital images are able to detect translocation [t(11;14)] multiple myeloma subtype, which is present in 15% to 24% of patients, shown to predict treatment response to Bcl-2 inhibitor therapy (such as venetoclax). A small cohort (n=25) of patients with t(11;14) have been compared to non-t(11;14) cases using the machine learning model and preliminary data indicate that there is a correlation between digital images and multiple myeloma subtype. In the future, we anticipate our AI model will improve the accuracy of diagnostic methods while reducing costs and offering deeper translational insights that will predict drug response *in vivo*.

Disclosures Landgren: *Merck:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring

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