

Dissecting the biology of lymphoid structures by SIMPEL algorithm

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Type selection

Choose your preferred presentation format: Poster

General data

Track: Adaptive Immunity

Topic: Systems immunology and Artificial Intelligence

Abstract text

Text: Lymphoid structures (LS) with active germinal centers (GC) represent highly organized immunological units where B-cell-associated immune responses develop and occur to produce high-affinity antibodies of various isotypes by plasma and memory B cells. LS are located not only in secondary lymphoid organs but are also formed ectopically in tissues with chronic inflammation and cancer. Formation of LS at the tumor site, where they are known as tertiary LS, was found to be associated with better clinical outcome in more than ten types of cancer. Important discoveries in respect of LS for colorectal cancer with liver metastasis are based on our research. To dissect the complex immunological imprint of LS, we developed and applied an integrative systems biology algorithm named SIMPEL – Systems Immunology-based Mapping of Patient-specific Expression Landscape. It consists of three synergistic modules: (i) spatial transcriptomics, where the mRNASeq is performed directly in FFPE tissue sections (Visium Spatial Gene Expression); (ii) compendium-wide analysis of curated transcriptomic datasets (GENEVESTIGATOR tool) and (iii) quantitative spatial tissue image cytometry (TissueFAXS platform). Spatial transcriptomics-based analysis of LS with GC, including tonsil specimens with classical LS and colon specimens with isolated LS, revealed top featured genes specifically characterizing a particular cluster. The LS-associated cluster(s) were thereby characterized by both the presence of classical B-cell markers as well as genes that are considered as novel candidates and subjected to the follow-up analysis. This includes the dissection of the global transcriptional landscape of the candidate gene across a multitude of anatomical parts and cell types as well as the analysis of the corresponding molecules on the protein level using quantitative tissue image cytometry. Overall, the combination of the individual modules allows to link the spatial gene and protein expression patterns to the tissue anatomy and cellular composition, by this dissecting novel aspects of LS biology.

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Conflict of Interest statement

Do you have any conflict of interest to declare?: No

Affirmation

- 1. Consent to participate and present onsite:** Yes
- 2. Consent to publication publication:** Yes
- 3. Consent on treatment of contact details saved in this system:** Yes