Quantification of neoantigen-mediated immunoediting in cancer evolution

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Abstract

Immunoediting, which includes three temporally distinct stages, termed elimination, equilibrium, and escape, has been proposed to explain the interactions between cancer cells and the immune system during the evolution of cancer. However the status of immunoediting in cancer remain unclear, and the existence of neoantigen depletion signal in untreated cancer has been debated. Here we developed a distribution pattern based method for quantifying neoantigen mediated negative selection in cancer evolution. Our method provides a robust and reliable quantification for immunoediting signal in individual cancer patient. The prevalence of immunoediting signal in immunotherapy untreated cancer genome has been demonstrated with this method. Importantly, the elimination and escape stages of immunoediting can be quantified separately, tumor types with strong immunoediting-elimination tend to have weak immunoediting-escape signal, and vice versa. Quantified immunoediting-elimination signal predicts cancer immunotherapy clinical response. Immunoediting quantification provides an evolutional perspective for evaluating the immunogenicity of neoantigen, and reveals potential biomarker for cancer precision immunotherapy.

Results

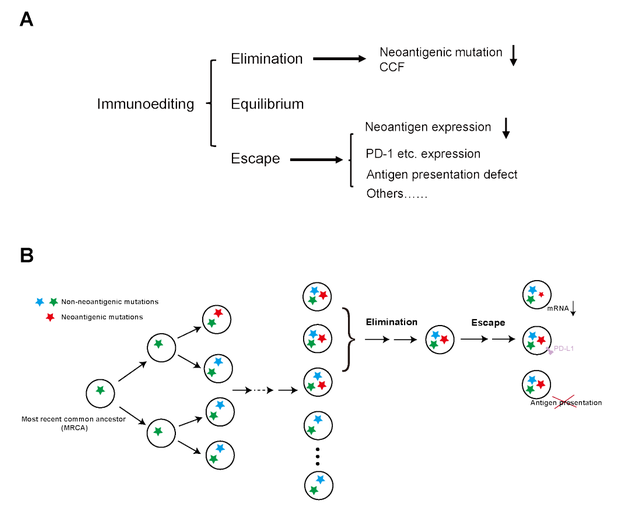

Figure 1: Conceptual framework for the quantification of elimination and escape phases of immunoediting.

Figure 2: Distribution pattern based method for the quantification of neoantigen mediated negative selection in cancer evolution.

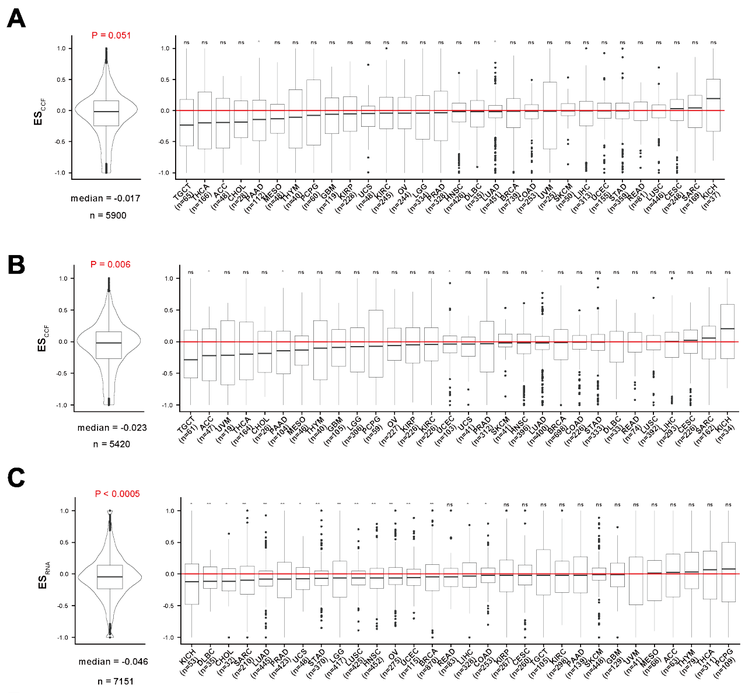

Figure 3: Pan-cancer distributions and features of the quantified immunoediting signals (ESCCF and ESRNA).

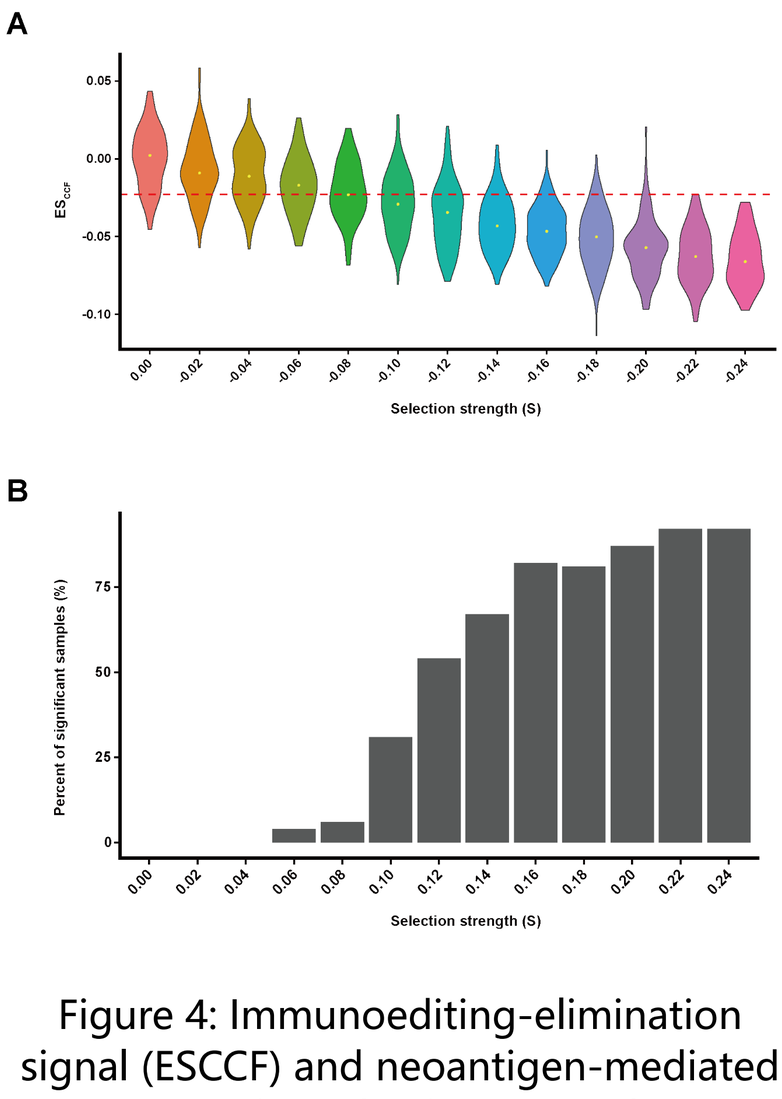

Figure 4: Immunoediting-elimination signal (ESCCF) and neoantigen-mediated negative selection strength quantification.

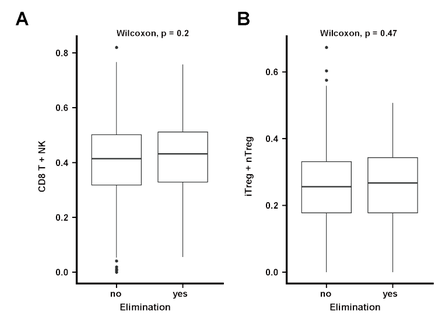

Figure 5: Immunoediting-elimination and escape signals and tumor immune cell infiltration status

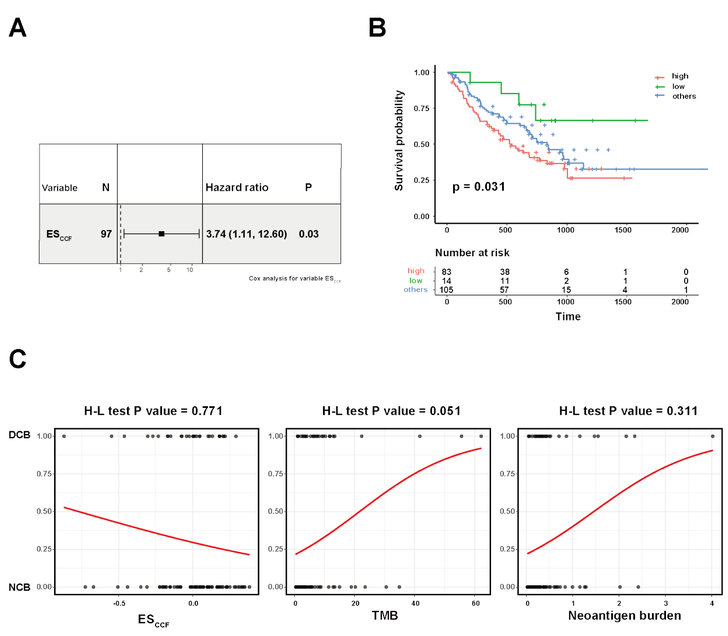

Figure 6: Quantified immunoediting-elimination signal (ESCCF) predicts cancer immunotherapy clinical response.

Conclusion

- Developed a brand new method for reliably quantifying neoantigen mediated immunoediting in individual cancer patient.
- With the new analysis framework, we demonstrate the pan-cancer existence of neoantigen mediated negative selection signal.
- Elimination and escape stages of immunoediting can be quantified separately, tumor types with strong immunoediting-elimination tend to have weak immunoediting-escape signal, and vice versa.
- Quantified immunoediting-elimination signal predicts cancer immunotherapy clinical response.

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