IgTreeZ: A toolkit for immunoglobulin gene lineage tree analysis

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Abstract

Somatic hypermutation (SHM) is an important diversification mechanism that plays a part in the creation of immune memory. Immunoglobulin (Ig) variable region gene lineage trees were used over the last four decades to model SHM and the selection mechanisms operating on B cell clones. We present IgTreeZ (Immunoglobulin Tree analyZer), a python-based tool that analyses many aspects of Ig gene lineage trees and their repertoires. Using simulations, we show that IgTreeZ can be reliably used for mutation and selection analyses. We used IgTreeZ on empirical data, found evidence for different mutation patterns in different B cell subpopulations, and gained insights into antigen-driven selection in corona virus disease 19 (COVID-19) patients. Most importantly, we show that including the CDR3 regions in selection analyses – which is only possible if these analyses are lineage tree-based – is crucial for obtaining correct results. Overall, we present a comprehensive lineage tree analysis tool that can reveal new biological insights into B cell repertoire dynamics.