Subclonal STAT3 Mutations Solidify Clonal Dominance.

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Supplemental Table 1. LGL Diagnostic Criteria

LGL diagnosis established by the presence of ≥ 3/5 of the following criteria:

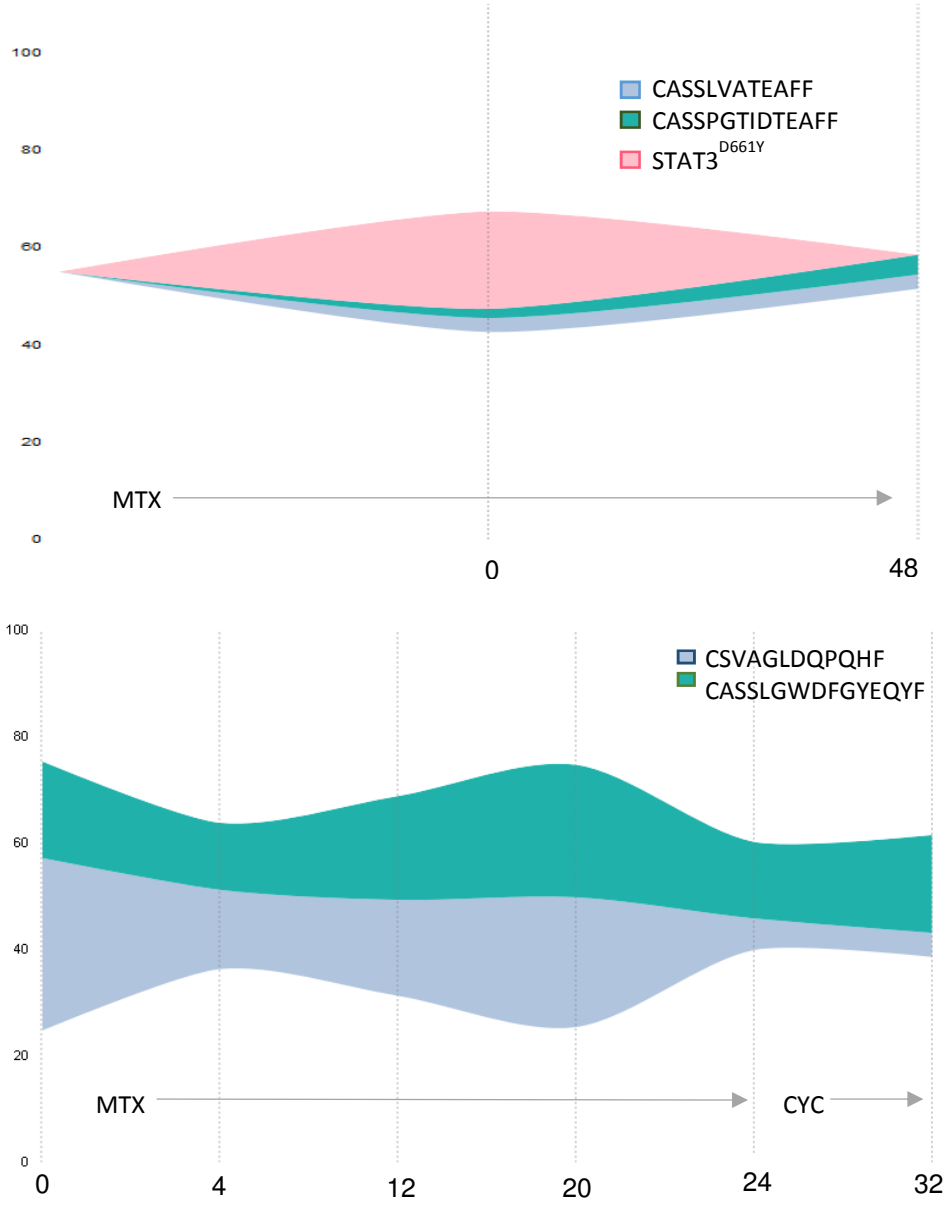
- LGL count >500/uL
- TCR rearrangement detected by PCR
- Presence of abnormal immunophenotype
- VB expansion by flow cytometry
- BM infiltration by LGL

Supplemental Table 2. T-LGL leukemia cohort characteristics (N=207)

Parameter	Value
Median AAD	61
Gender	110M :97F
Median FU	40 Months
T-LGL	92%
NK-LGL	8%
TCR Rearrangement by PCR	95%
VB Skewing	
TCR Deep Sequencing	23%
Longitudinal	10%
STAT3 Deep Sequencing	100%
Longitudinal	44%
STAT3 Mutation	38%
Y640F	42%*
D661Y	34%*
D661V	11%*
N647I	8%*
Hematologic Manifestation	
Asymptomatic	8%
Anemia	53%
Neutropenia	46%
Thrombocytopenia	24%
Multilineage Cytopenia	26%
Pancytopenia	9%
Response to IST	
CSA	29/75 (39%)
CYC	24/52 (46%)
MTX	26/69 (37%)

AAD- age at diagnosis, FU-Follow-up, CSA-cyclosporine, CYC-cyclophosphamide, MTX- methotrexate
*% of mutant cases

Supplemental Figure 1. Clonal dynamics of TCR clonotypes throughout clinical course of NK-LGL patients. Fish plots depicting the clonal expansions of 2 NK-LGL patients. Sampling time points are shown along the X-axis and the clonal burden is shown on the Y-axis.



Supplemental Figure 2. Depiction of the oligoclonal skewing of TCR clonotypes during disease manifestation of T LGL. The clonal expansion can be visualized as each sphere represents a clone and each color represents a clone with a specific CDR3 "biological barcode". Following treatment, three scenarios can be seen: in responders (a) contraction or (b) silencing, and in non-responders (a) clonal persistence or (b) the expansion of a previously minor clonotype. MT signifies a STAT3 mutation. Tx-treatment.