



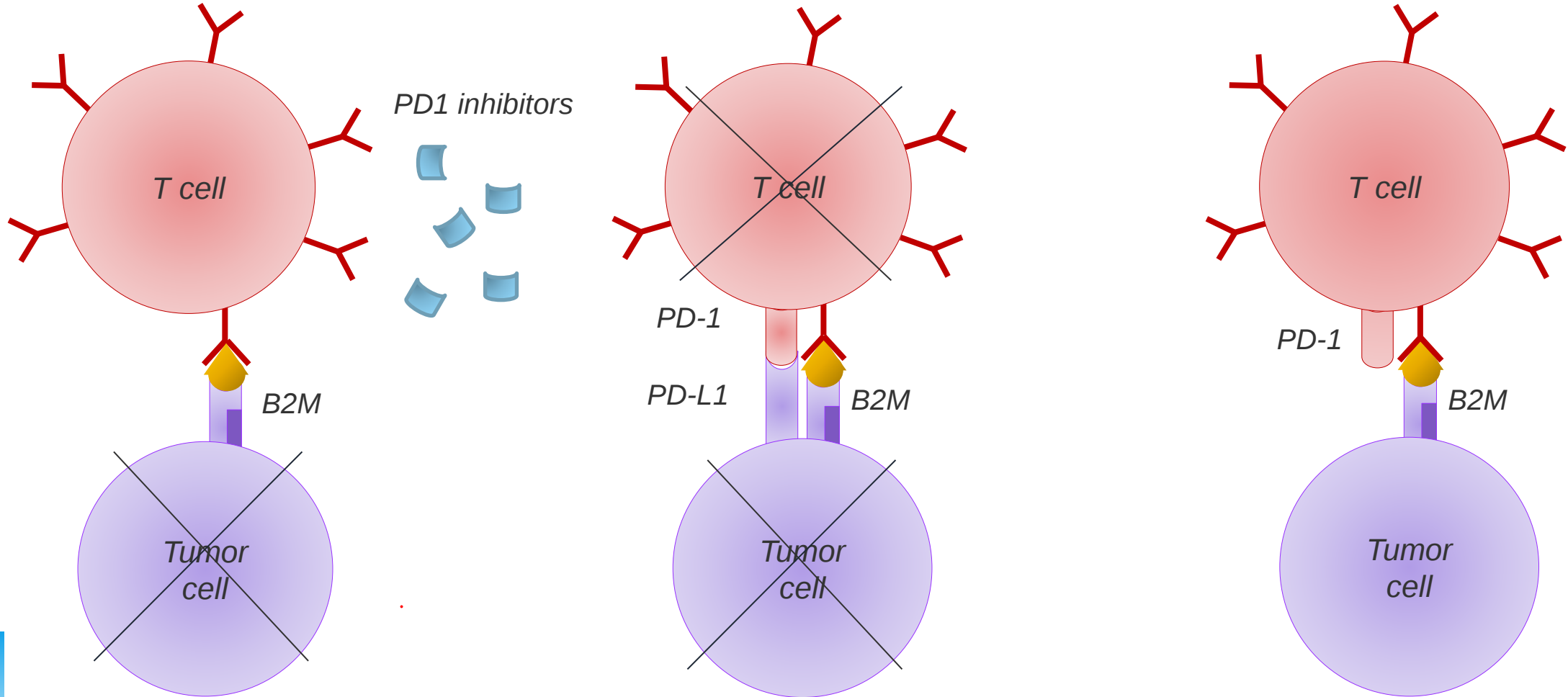
Lynch syndrome-associated epithelial ovarian cancer and its immunological profile

Maria Rasmussen

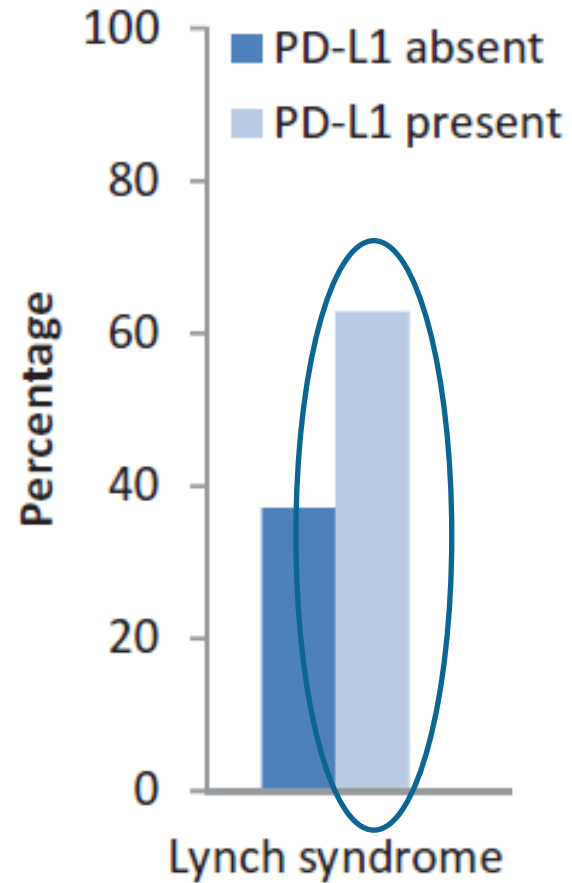
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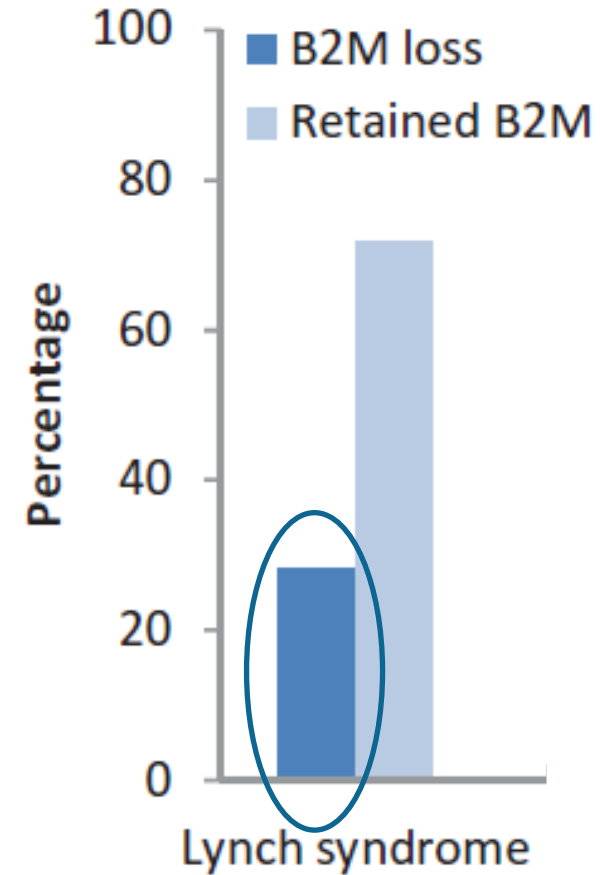
Immune response and immune evasion



Immune response and immune evasion



Edited from Walkowska et al. 2019



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Aim

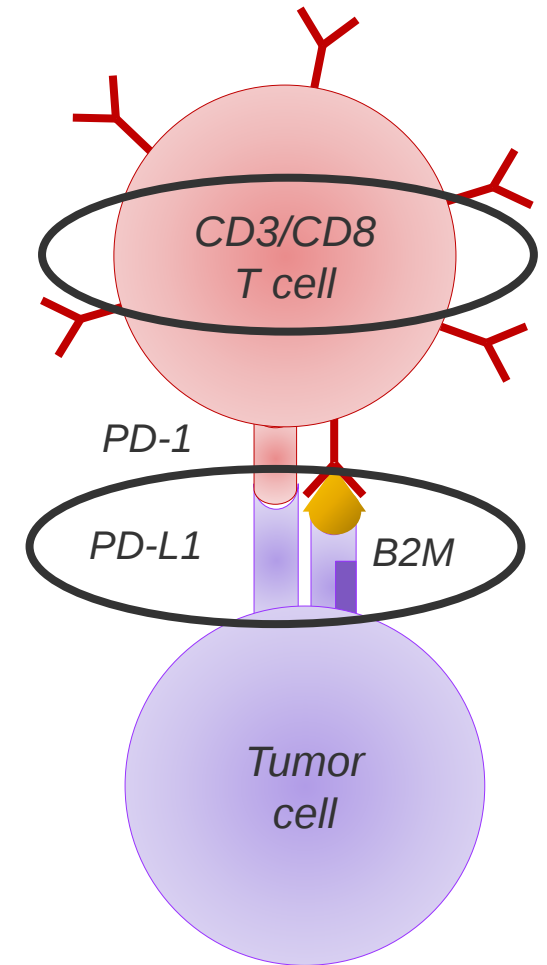
Investigate the immune response

CD3⁺ and CD8⁺ tumor-infiltrating lymphocytes (TILs)

Investigate possible immune evasion mechanisms

Expression of Programmed death 1 ligand 1 (PD-L1)

Loss of expression of beta-2 microglobulin (B2M)



The epithelial ovarian cancer cohort

87 epithelial ovarian tumors identified in the Danish HNPCC Register



60 tumors were surgically removed and possible to collect



35 tumors were collected



30 samples with sufficient tumor tissue

The epithelial ovarian cancer cohort

Mean age at diagnosis (N=30):

- 47.3 years (30–69)

MMR gene distribution (N=30):

- MSH2: 60%
- MSH6: 33%
- MLH1: 3%
- PMS2: 3%

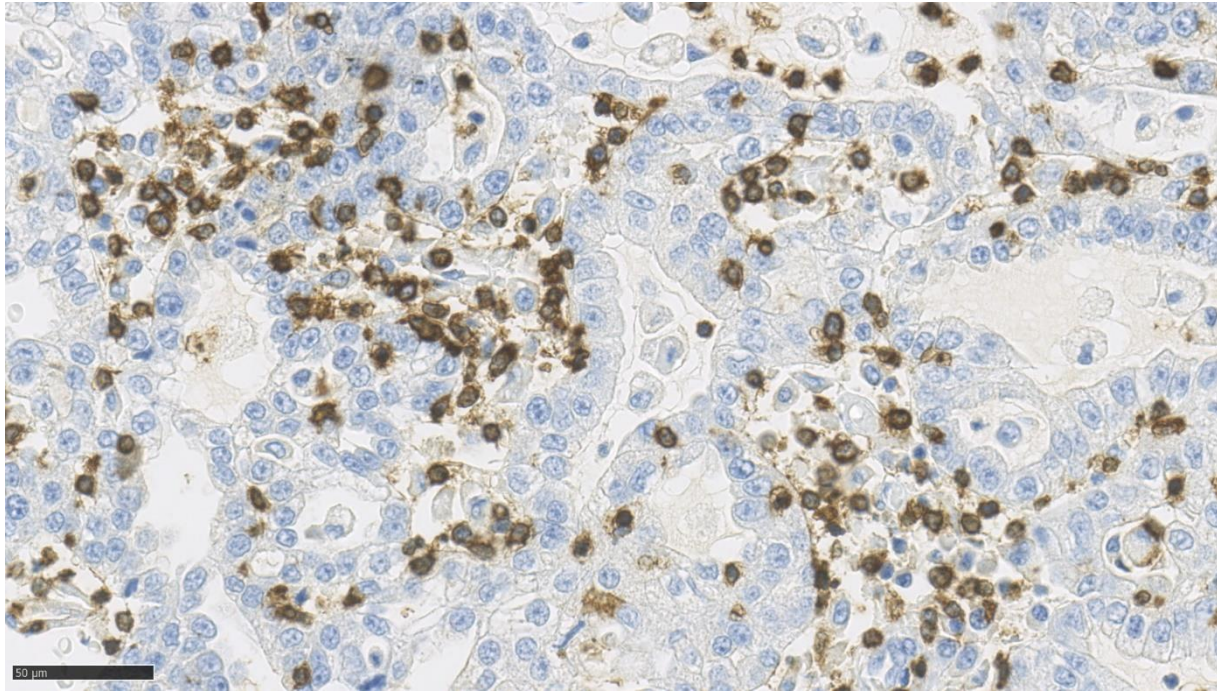
Stage (N=28):

- I–II: 89%
- III–IV: 11%

Morphology (N=27):

- Endometrioid: 56%
- Clear cell: 22%
- Mucinous: 11%
- Serous: 11%

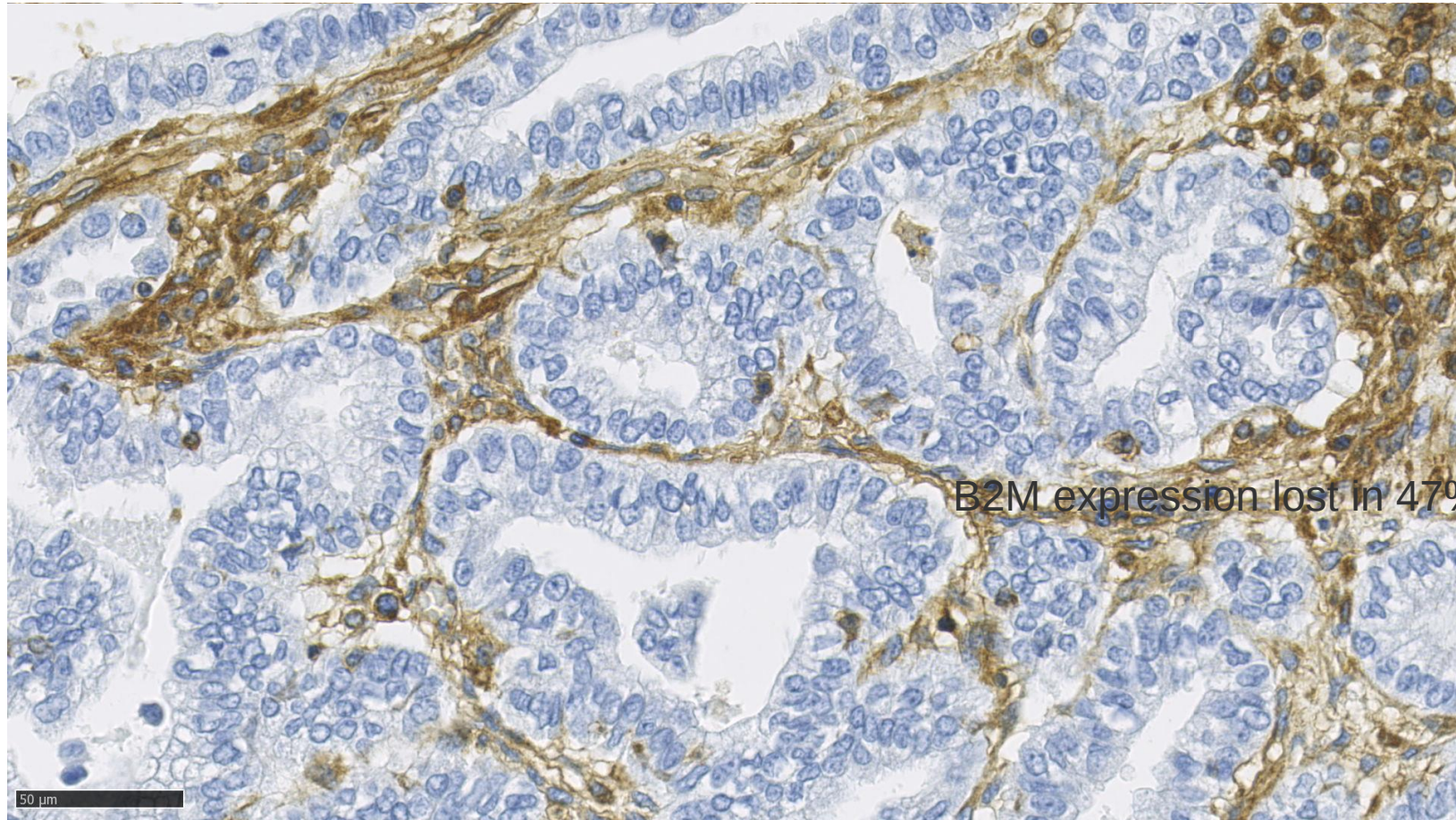
High levels of TILs



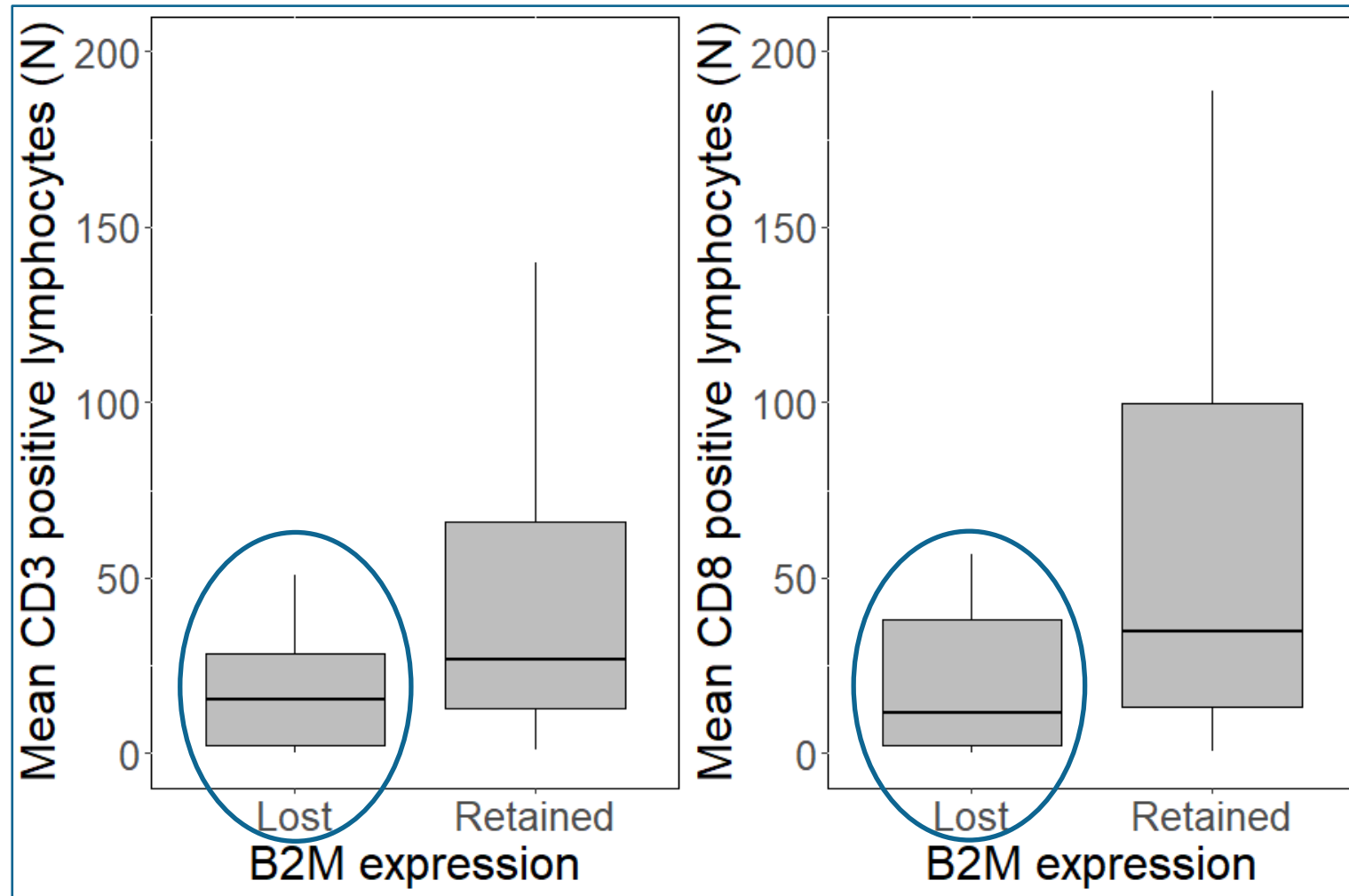
CD3-positive: 60% of the tumors

CD8-positive: 53% of the tumors

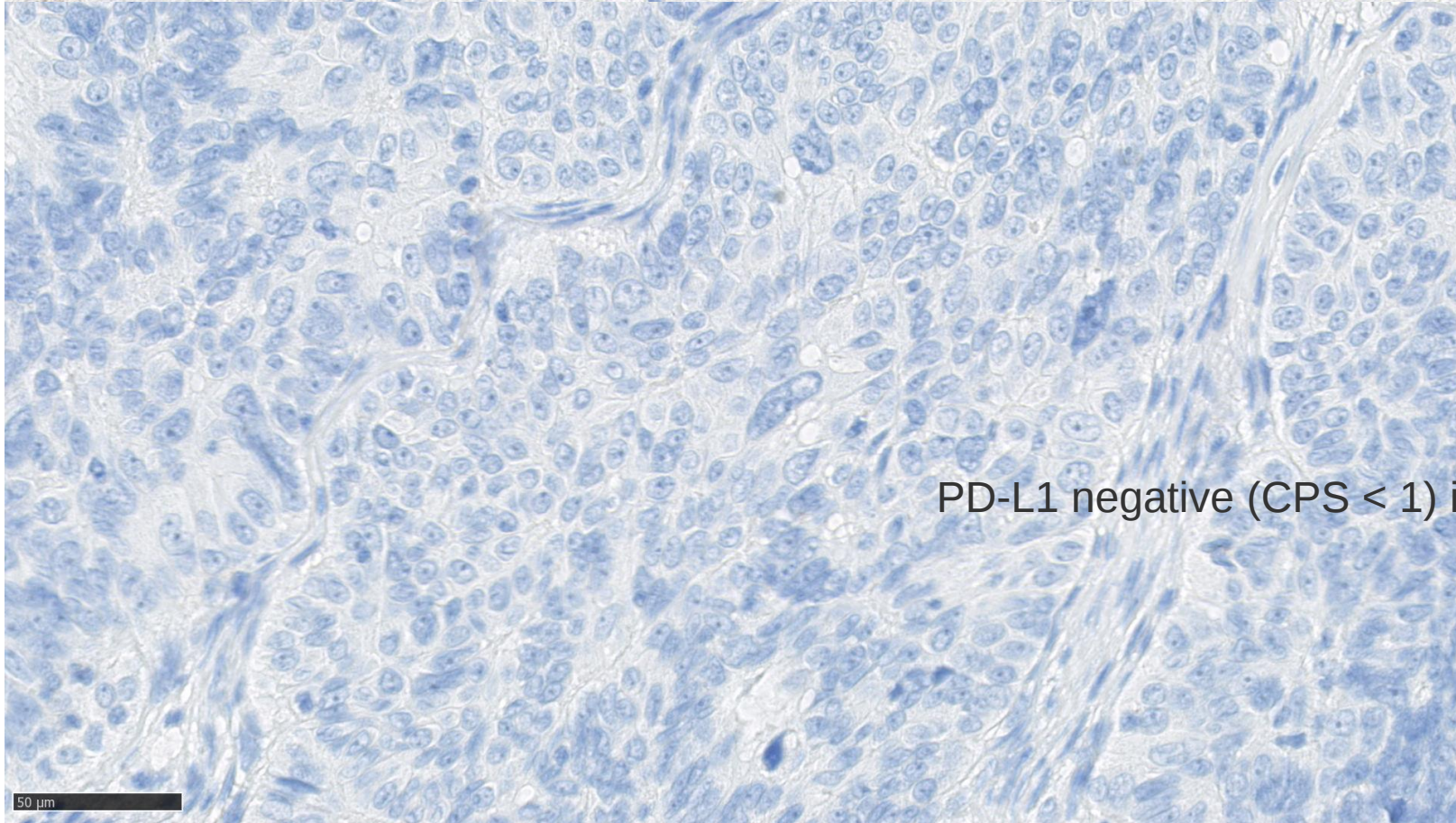
Immune evasion via B2M loss



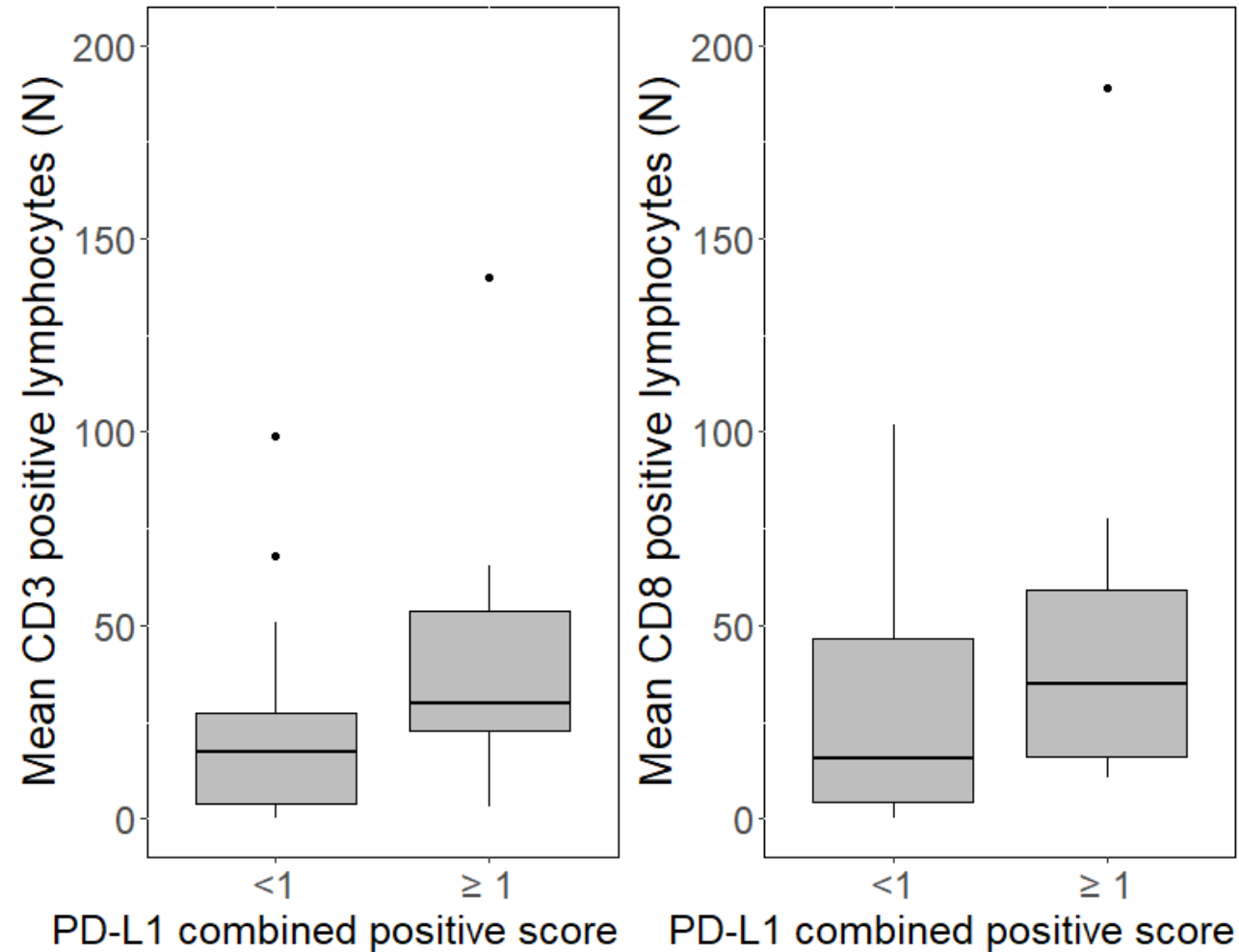
No association between B2M loss and TILs



Immune evasion via PD-L1 expression



No association between PD-L1 expression and TILs



Concordance between microsatellite instability (MSI) and mismatch repair-deficiency (MMR-deficiency)

MMR immunohistochemistry (N=29):

- Loss of MMR protein expression: 93%

MSI (N=26):

- MSI-high: 54%

Both MMR immunohistochemistry and MSI (N=25)

- 60% concordance

Conclusion

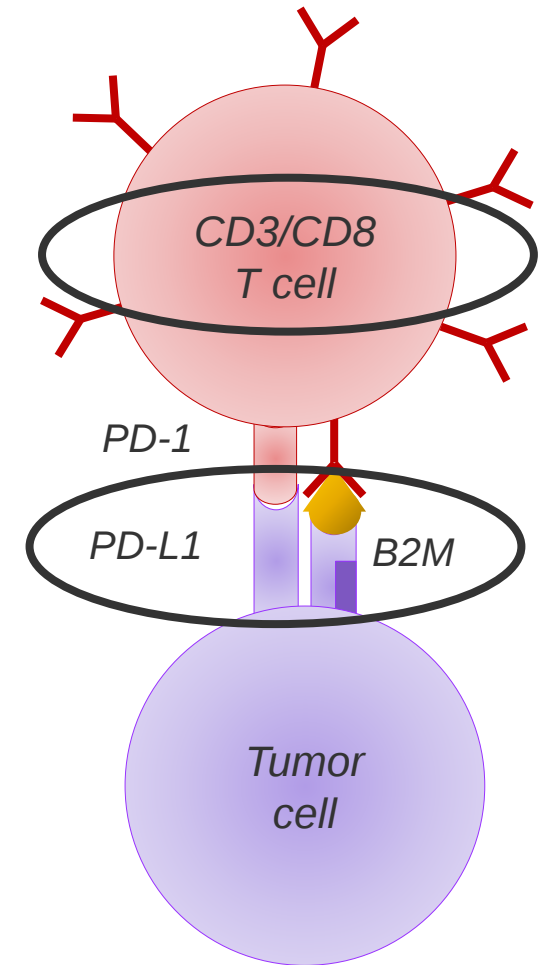
>50% showed high infiltration of lymphocytes

Frequent immune evasion via

PD-L1 upregulation (28%)

B2M loss (47%)

Loss of B2M may be a general immune evasion mechanism among Lynch syndrome cancers and may cause resistance towards immunotherapy.



Low concordance between IHC and MSI



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