3. Was the Patient Immune Profile Altered by Treatment?

**Model of tumor inflammation**

![Image: Pathways analyses](Image)

**Analysis of patient serum data post-treatment indicates an active effect of CLBS20 compared to control**

**Pathways analyses**
- Tumor and inflammation markers increased to suggest natural tumor progression.
- IL-12p40 and IL-17f upregulated in CLBS20 arm.
- Post-treatment evaluation 4 weeks:
  - IL-23p19
  - IL-6
  - IFN-γ
  - IL-17A

**Evaluation of specific pathways, post-treatment**
- **Control arm:**
  - Tumor and inflammation markers increased from baseline.
- **CLBS20 arm:**
  - Tumor markers were only slightly increased from baseline.
  - The majority of inflammatory pathways decreased from baseline.
  - A few pathways only slightly elevated from baseline, suggestive of MOA.

**Statistical analyses of high and low survivor groups in CLBS20 treatment arm at 4 weeks after first administration of CLBS20**

- **High survivors**
  - Fold difference: -6.44 -46.42 -6.14 -5.72 -9.67 -12.01 -159.70 -5.94 -14.88 -46.20
  - *p* values: 0.024 0.038 0.047 0.031

- **CLBS20 arm:**
  - Post-treatment evaluation 4 weeks:
    - IL-12p40: 7.822E-04 1.56E-03
    - IL-17f: 3.423E-06 1.51E-06

**Pathways involved in tumor hierarchy and molecular mechanisms**
- **Angiogenesis**
  - Tumor prevalence
  - Percent change from baseline
  - Control (n=20) vs. CLBS20 (n=20)

**Conclusions**
- **Immunological modeling and testing**
  - Interaction models can be constructed from published knowledge and the measured patient values of individual stimulus effect markers.
  - Linear regression models using machine learning tools are used to verify/validate a model.
  - Based on observations in the treatment group (CLBS20), we constructed pathway models and performed survival analysis as a dependent variable.

**Immunological modeling and testing**

- **The CLBS20 treatment**
  - Associated with reduced tumor progression and reduced inflammation, with some of the markers at statistical significance.
  - The control arm did not show the same effect.
  - The CLBS20 treatment is associated with reduced tumor progression and increased inflammation, with some of the markers at statistical significance.
  - The control arm did not show the same effect.

- **The Th17 pathway**
  - Associated with higher tumor and immune response, suggestive of a possible involvement in MOA.