



aGvHD

## Predictive plasma-based protein biomarkers for patients with acute graft-versus-host disease



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Acute graft-versus-host disease (aGvHD) is a multisystem disorder that is a common complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT) and is a reaction between donor immune cells and host tissues. Recent studies have identified predictive plasma biomarkers present before aGvHD onset as potential predictive biomarkers in order to improve early and accurate diagnosis of the condition and start efficient preemptive immune suppressive therapy to reduce the intensity of tissue damage.

In this study, [Jungcheon Shin](#) and colleagues used an unbiased proteome profiling method to analyze prospectively collected plasma samples from allo-HSCT recipients to identify potential protein biomarkers that predict the risk of aGvHD and non-relapse mortality (NRM). The authors [published](#) their paper in a recent issue of *Blood Cells, Molecules and Diseases*.

### Patients and methods:

The study included a discovery and validation phase.

#### Discovery cohort

- N = 5 aGvHD patients
- N = 5 control patients
- Median age = 32 years (range, 16–57)
- Proteome profiling of plasma samples were collected and analyzed

#### Validation cohort

- N = 89 patients
- Median age = 44 years (range, 16–64)
- The predictive value of the identified candidate biomarkers was assessed regarding aGvHD and NRM risk

### Key findings:

- Seven candidate proteins were identified in patients in the discovery cohort

- Forty patients (44.9%) developed aGvHD in the validation cohort
  - Grade I: 9 patients (10.1%)
  - Grade II: 14 patients (15.7%)
  - Grade III: 12 patients (13.5%)
  - Grade IV: 5 patients (5.6%)
- Higher levels of the identified proteins showed correlation with a higher risk of aGvHD and NRM in comparison with low levels of the proteins in post-engraftment plasma samples
- The following biomarkers were identified as potential predictive markers and were used as biomarker panel scores (range, 0–3):
  - Tissue inhibitor of metalloproteinase 1
  - Plastin-2
  - Regenerating islet derived protein 3- $\alpha$
- The biomarker panel score showed significant correlation with aGvHD and NRM risk
- Association of biomarker panel score with cause-specific risk of aGvHD and NRM
  - aGvHD risk: HR = 1.57 (95% CI, 1.13–2.18),  $P = 0.008$
  - NRM risk: HR = 2.68 (95% CI, 1.57–4.59),  $P < 0.001$
- Prediction of aGvHD and NRM was significantly improved with the biomarker panel score in combination with clinical predictors

This study showed that plasma-derived protein biomarkers can predict aGvHD and NRM before the onset of clinical symptoms. To date, this is the first study that used a LC-MS/MS-based quantitative proteome profiling method, which is currently “state-of-the-art in proteomics research” to evaluate a predictive biomarker panel for aGvHD by analyzing plasma samples obtained at the preclinical stage.

## References

1. Shin J. *et al.* Plasma-based protein biomarkers can predict the risk of acute graft-versus-host disease and non-relapse mortality in patients undergoing allogeneic hematopoietic stem cell transplantation. *Blood Cells Mol Dis.* 2018 Oct 4. DOI: [1016/j.bcmd.2018.10.001](https://doi.org/10.1016/j.bcmd.2018.10.001). [Epub ahead of print].