

Briefing Doc: Molecular Characterization and Therapeutic Outcomes in Pediatric Aplastic Anemia

Source: Adhikari, S., Nayek, K., Bandyopadhyay, A., & Mandal, P. (2021). Implication of therapeutic outcomes associated with molecular characterization of paediatric aplastic anaemia. *Biochemistry and Biophysics Reports*, 25, 100899.

Main Themes:

- **Molecular characterization** of telomere length and mesenchymal stem cells (MSCs) gene expression can inform treatment strategies for pediatric aplastic anemia (AA).
- **Leucocyte telomere length** is a potential biomarker for predicting response to therapy.
- **Gene expression profiling** of MSCs reveals differentially expressed genes associated with therapeutic outcomes.

Key Findings:

- **Telomere Length:** Pediatric AA patients displayed significantly shorter telomeres compared to healthy donors.
- A subgroup of patients (20%) exhibited moderate telomere length, comparable to healthy donors. **"Telomere length estimation revealed that telomere length was significantly (p-value < 0.001) reduced in aplastic anaemia patients compared to healthy donors. Interestingly, 2 out of 10 patients (2/10, 20%) showed moderate telomere length compared to age-matched healthy donors and no indication of regression in telomere length was found."**
- **TERF2 Gene Expression:** TERF2, a gene involved in telomere maintenance, was significantly downregulated in patients with shorter telomeres but not in those with moderate telomere length. **"Among these 9 genes, only 1 gene (TERF2) revealed significant downregulation among case samples with shorter telomere length (fold change = -3.52-fold, p = 0.01) compared to healthy donors but not among cases with moderate telomere length."**
- **MSC Gene Expression Profiling:** Three genes (GAS2L3, MK167, and TMSB15A) were significantly downregulated in patients who responded to immunosuppressive therapy but not in one patient who required bone marrow transplantation. **"MSCs gene expression profiling revealed that three genes (GAS2L3, MK167, and TMSB15A) were downregulated among the patients with immunosuppressive therapy but not among one patient with bone marrow transplantation."**
- The AGT gene, involved in angiotensinogen production, was consistently downregulated across all AA patients.

Implications for Treatment:

- **Telomere Length:** Shorter telomere length may indicate eligibility for treatment with Danazol, a drug effective in telomere disorders.
- **TERF2:** Downregulation of TERF2 could be a biomarker for identifying AA subsets and a potential therapeutic target.

- **GAS2L3, MK167, and TMSB15A:** Expression levels of these genes may predict response to immunosuppressive therapy and guide treatment decisions.

Future Directions:

- Further investigation into the roles of identified genes and their potential as therapeutic targets.
- Development of personalized treatment strategies based on molecular characterization.
- Exploration of novel therapies, such as small molecule inhibitors and miRNA-based approaches.

Overall, this study highlights the importance of molecular characterization in understanding the pathogenesis of pediatric AA and developing effective treatment strategies. The identification of potential biomarkers associated with therapeutic outcomes holds promise for improving diagnosis and personalized management of this disease.