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ORIGINAL ARTICLE

RNA sequencing indicates distinct platelet transcriptomic changes in immune thrombocytopenia

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Abstract

Background: In immune thrombocytopenia (ITP), platelet-intrinsic alterations and their potential contribution to disease pathogenesis remain incompletely understood. Since platelets, although anucleate, retain a functional transcriptome, transcriptomic profiling may provide insight into disease-associated changes.

Objectives: To investigate platelet-intrinsic transcriptomic changes in ITP and to determine whether these alterations are disease-specific compared with non-ITP.

Methods: Total RNA sequencing was performed on purified platelets from patients with active ITP (n = 6), chemotherapy-induced thrombocytopenia as a non-ITP control (n = 6), ITP in treatment-free remission (n = 6), and healthy controls (n = 8).

Results: Platelets from patients with active ITP exhibited higher total RNA content, consistent with enrichment of young, recently released platelets. Transcriptomic analysis identified a profile dominated by platelet activation pathways, including integrin- and calcium-dependent signaling, cytoskeletal remodeling, and vesicle trafficking. In contrast, genes involved in mitochondrial biogenesis and oxidative phosphorylation were downregulated, accompanied by a reduced proportion of

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mitochondrial-derived RNA. Although both active ITP and chemotherapy-induced thrombocytopenia showed elevated RNA content relative to healthy controls, reflecting enhanced platelet turnover, the coordinated upregulation of activation-associated transcripts was unique to active ITP. Platelets from ITP patients in treatment-free remission showed partial normalization of the transcriptional profile, with loss of the activation signature and intermediate expression patterns between active ITP and healthy controls.

Conclusion: RNA sequencing data show distinct platelet transcriptomic changes in ITP, marked by coordinated upregulation of platelet activation pathways and reduced mitochondrial gene expression. This profile is consistent with an activation-primed, metabolically altered platelet state and may reflect disease-related changes in platelet biology in ITP.

KEYWORDS
blood platelets, immune thrombocytopenia, platelet activation, RNA sequencing, transcriptome

1 | INTRODUCTION

Immune thrombocytopenia (ITP) is an autoimmune disease characterized by isolated thrombocytopenia due to increased platelet clearance and impaired megakaryopoiesis. Clinically, ITP manifests primarily through bleeding of variable severity [1].

The pathophysiology of ITP is driven by complex immune dysregulation, including antibody-mediated platelet destruction, alterations in megakaryocyte biology, and T-cell–driven immune mechanisms [2]. Although immune dysregulation in ITP has been extensively characterized, the platelet-intrinsic contribution to disease pathogenesis remains poorly understood. Platelets in ITP have traditionally been considered primarily targets of immune-mediated destruction rather than active participants in the disease process. However, advances in platelet biology increasingly challenge this view, underscoring their pivotal roles not only in hemostasis but also in inflammation and immunity [3,4]. For example, platelets have been shown to directly interact with immune cells, including $CD4^+$ and $CD8^+$ T lymphocytes, and to participate in inflammatory signaling processes [5–8]. Expression of major histocompatibility complex class I on platelets enables modulation of T-cell activation and has been implicated in proinflammatory T-cell differentiation [5]. In addition, platelets contribute to immune signaling by releasing platelet-derived microparticles that contain cytokines and autoantigens and can modulate immune responses [9,10].

At the molecular level, anucleate platelets retain a complex transcriptome inherited from megakaryocytes [11]. This RNA repertoire comprises coding, noncoding, and mitochondrial transcripts and reflects both megakaryocytic programming and regulatory influences in circulation [12]. In several disease contexts, transcriptomic analyses have revealed altered platelet RNA signatures, including cardiovascular disease, cancer, and sepsis [13–18]. For ITP, however, such analyses remain scarce, presumably due to technical challenges associated with the limited amounts of starting material available from thrombocytopenic patients.

Here, we performed total RNA sequencing of highly purified platelets from patients with active ITP to enable transcriptome-wide characterization of this disease. We examined whether platelets from ITP patients display transcriptomic differences relative to healthy controls and evaluated the disease specificity of the identified signatures by comparing them with chemotherapy-induced thrombocytopenia as a non-ITP control.

2 | METHODS

A total of 26 individuals were enrolled: 6 patients with active ITP without ITP-specific treatment at sampling (median platelet counts (PLT) 35×10^9/L); 6 patients with chemotherapy-induced thrombocytopenia during marrow recovery as platelet-matched non-ITP controls (median PLT 37×10^9/L); 6 ITP patients in treatment-free remission (median PLT 178×10^9/L); and 8 healthy controls (median PLT 229×10^9/L). Groups were balanced for age and sex (Supplementary Table S1).

ITP diagnosis was established according to current international consensus criteria [19]. All included patients had primary ITP. Active ITP patients had both newly diagnosed and persistent/chronic ITP. At the time of sampling, they were either under a watch-and-wait approach or before initiating ITP-specific therapy; none had previously received any ITP-directed therapy other than corticosteroids. Patients in remission had stable PLT $> 100 \times 10^9$/L for at least 3 months without ongoing ITP-directed therapy; prior treatments included corticosteroids and thrombopoietin (TPO) receptor agonists. Patients with chemotherapy-induced thrombocytopenia were sampled during marrow recovery, with PLT approximating those of the active ITP cohort, resulting in comparable median platelet counts between groups.

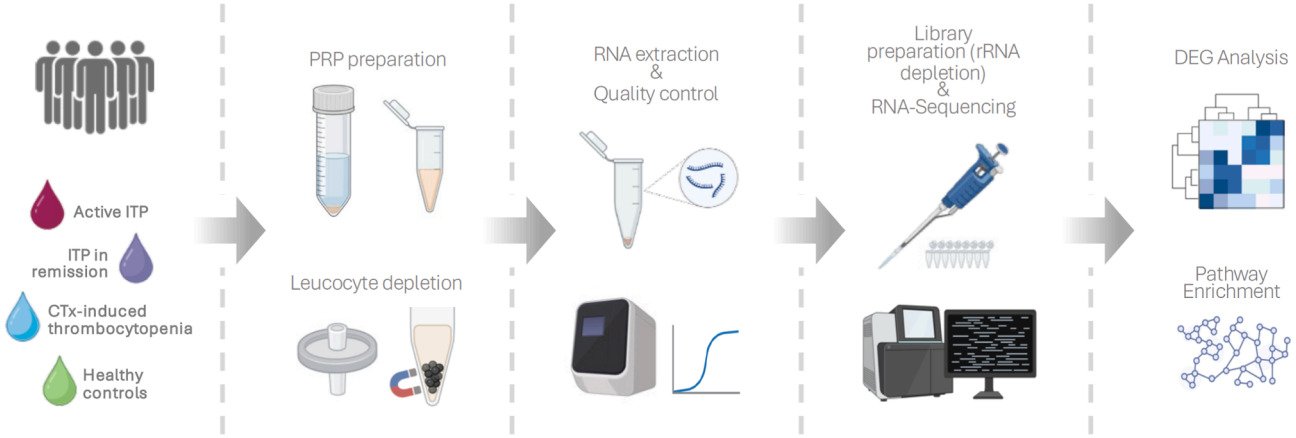


FIGURE 1 Schematic overview of the platelet RNA-sequencing workflow. Platelet-rich plasma (PRP) was prepared from individuals with active immune thrombocytopenia (ITP), ITP in remission, chemotherapy (CTx)-induced thrombocytopenia, and healthy controls. After leukocyte depletion, platelet RNA was extracted, quality-controlled, and subjected to ribosomal RNA (rRNA)-depletion-based library preparation, followed by high-throughput sequencing. Differentially expressed genes (DEG) and pathway enrichment analyses were performed. Parts of Figure 1 were created in BioRender.

A minimum PLT of 20 × 10^9/L was required to ensure an adequate RNA yield. Peripheral blood (36 mL) was collected in EDTA and processed immediately after venipuncture to prevent *in vitro* platelet activation. Platelet-rich plasma was obtained by sequential centrifugation as previously described [20]. A platelet inhibition cocktail was prepared in Dulbecco's phosphate-buffered saline (DPBS, without calcium and magnesium; Gibco, Thermo Fisher Scientific) containing 0.25 mM EDTA, 10 μM prostaglandin E_1 (PGE_1), and 0.05% (w/v) bovine serum albumin (BSA). One milliliter of this cocktail was added to 10 mL of plasma during platelet-rich plasma preparation. Platelets were pelleted and further purified using a 2-step leukocyte-depletion protocol consisting of filtration (Acrodisc WBC Syringe Filter, Pall Corporation) and CD45-targeted magnetic bead separation ((CD45 MicroBeads, Miltenyi Biotec). Total RNA was extracted using the mirVana miRNA Isolation Kit (Thermo Fisher Scientific). RNA concentration was measured using the Qubit RNA HS Assay (Thermo Fisher Scientific). After CD45 bead depletion, the final volumes were 50 μL, with RNA concentrations ranging from 2 to 19.7 ng/μL. Platelet-specific transcripts (*P2RY1* and *ITGA2B*) and leukocyte/erythrocyte markers (*PTPRC* and *GYPA*) were assessed by quantitative polymerase chain reaction (qPCR) to confirm sample purity and RNA yield. For library preparation, 50 ng of total RNA per sample was processed using the RNA Library Prep Kit with Polaris Depletion (Watchmaker Genomics). Adapter ligation was performed with 1 μM xGen Stubby Adapters (Integrated DNA Technologies), followed by double postligation clean-up. Libraries were amplified by polymerase chain reaction for 13 cycles and sequenced on an Illumina NovaSeq 6000 (200 cycles, paired-end reads). Library preparation and sequencing were performed in 2 batches, with samples from all 4 groups distributed across both batches to avoid batch-group confounding.

Reads were aligned to the human reference genome (GRCh38/hg38) using STAR (v2.7.10b) [21] with Ensembl release 104 splice annotations [22], with parameters optimized for unique alignments. Gene-level counts were generated with featureCounts (v2.0.1) [23] and normalized using DESeq2 (v1.38.3) [24] in R (v4.2.2, R Core Team, R Foundation for Statistical Computing) to account for differences in library depth and composition. Principal component analysis (PCA) of the 500 most variable genes did not show clustering by batch (Supplementary Figure S1A). Differentially expressed genes (DEGs) were identified using the Wald test with sex as a covariate, and *P* values were adjusted for multiple testing using the independent hypothesis weighting (IHW) method, implemented with the IHW Bioconductor package (v1.26.0) [25]. Genes with an adjusted $P \leq .05$ were considered significant. Functional enrichment of DEGs was evaluated using the Gene Ontology, Kyoto Encyclopedia of Genes and Genomes (KEGG), and Reactome frameworks implemented in a Python-based workflow (Python v3.10, GSEApy v1.1.8 [26], and pandas v2.2.2 [27]).

A schematic overview of the workflow is provided in Figure 1.

This study was approved by the local ethics committee of the Technical University Dresden, Germany (approval number: BO-EK-572122021), and all patients and healthy control subjects provided written informed consent in accordance with the Declaration of Helsinki.

3 | RESULTS

3.1 | RNA yield and global transcriptomic profiling

Relative to peripheral PLT, the median RNA yield was highest in active ITP and chemotherapy-induced thrombocytopenia, indicating enrichment of young, RNA-rich platelets in both thrombocytopenic groups (Supplementary Table S1). Sequencing produced high-quality libraries (mean, 60.7 million paired-end reads per sample and >90%

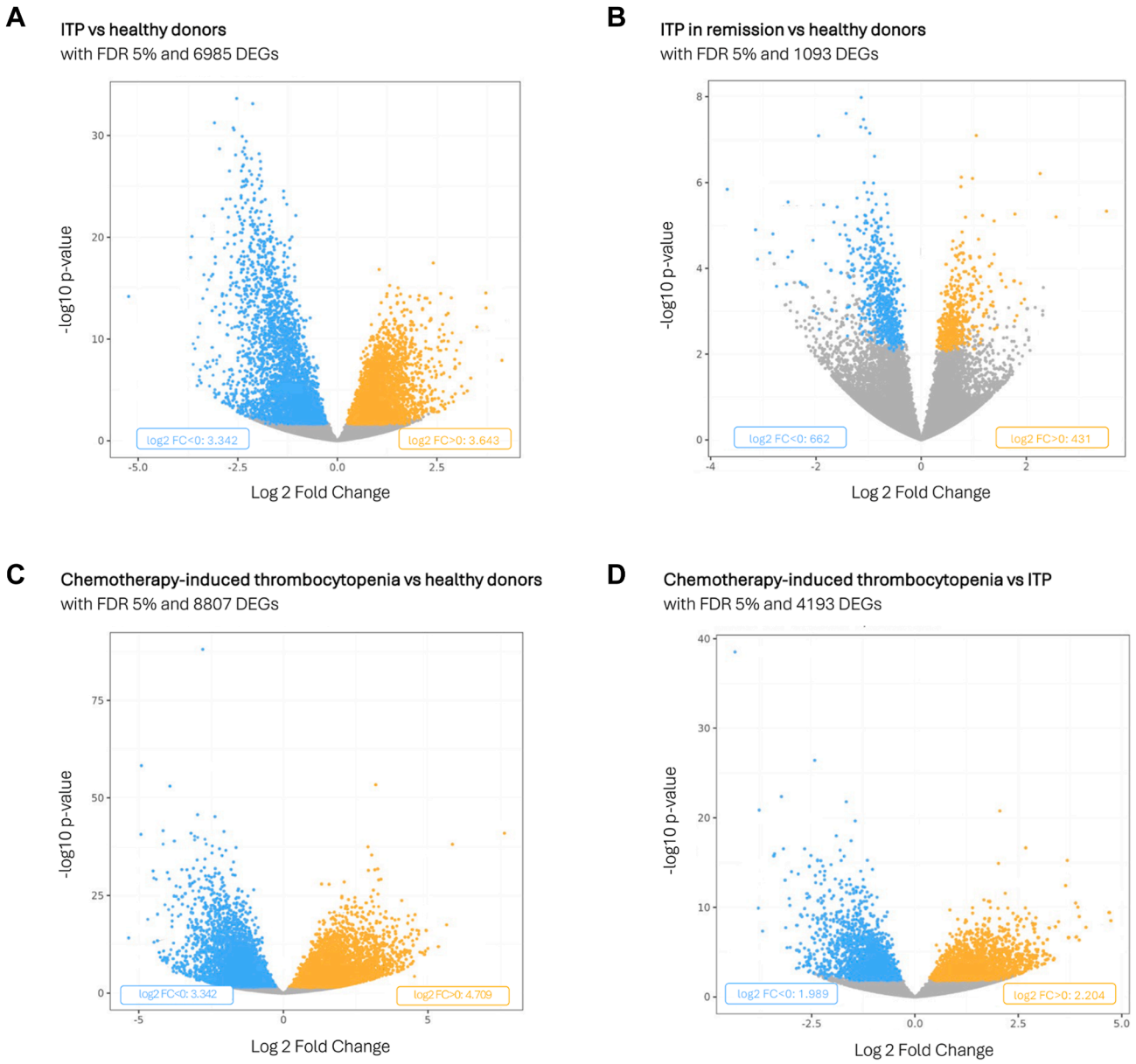


FIGURE 2 Differentially expressed platelet transcripts across disease groups. Volcano plots for (A) immune thrombocytopenia (ITP), (B) ITP in remission, (C) chemotherapy-induced thrombocytopenia vs healthy donors, and (D) chemotherapy-induced thrombocytopenia vs ITP. X-axis: $\log_2$-fold change (FC); y-axis: $-\log_{10}$ FC *P* value (y-axis scaling differs between panels). Transcripts with a false discovery rate (FDR) < 5% are shown in orange (upregulated) or blue (downregulated); nonsignificant transcripts are in gray. The number of differentially expressed genes (DEGs) per comparison is indicated.

unique mapping; median, 5864 transcripts with ≥1 counts per million. Platelet purity was confirmed by high expression of PPBP and platelet factor 4, and very low expression of leucocyte- and erythrocyte-specific markers (PTPRC, CD14, and HBB < 0.05% relative to PPBP; Supplementary Table S2). Expression profiles of healthy control platelets closely matched those of reference platelet RNA sequencing datasets [28,29], with the expected ranking of the most abundant platelet markers and a high intersample Spearman correlation among healthy controls (ρ = .93-.97). PCA showed disease-associated separation, with ITP remission samples displaying an intermediate profile between active ITP and healthy controls (Supplementary Figure S1B). Differential expression analysis revealed distinct transcriptional signatures among groups (Figure 2; detailed results are in Supplementary Tables S3–S13).

3.2 | Platelet activation pathways are upregulated in active ITP

To identify transcriptional changes in active ITP, platelet transcriptomes were first compared between patients with active ITP and healthy controls. Differential expression analysis identified 3643 significantly upregulated and 3342 significantly downregulated transcripts in ITP platelets. Pathway enrichment consistently revealed a pronounced platelet

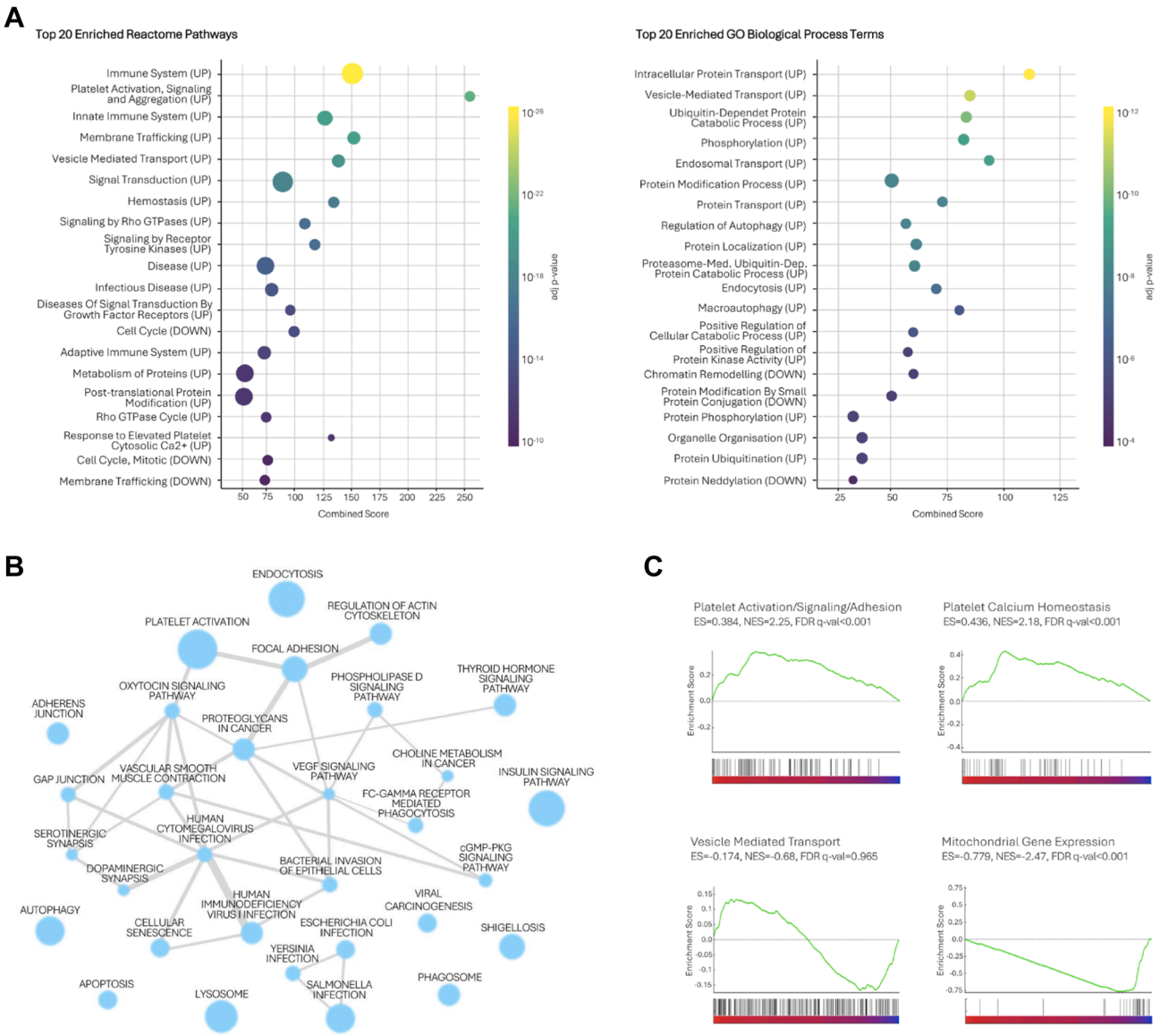


FIGURE 3 Functional pathway and gene set enrichment analyses of platelet transcripts in immune thrombocytopenia (ITP). (A) Functional enrichment analysis of differentially expressed platelet transcripts in ITP vs healthy controls. Shown are the top 20 enriched Reactome pathways and Gene Ontology (GO) Biological Process terms. Enrichment direction (UP or DOWN) is indicated in parentheses. Dot size indicates the number of overlapping genes, color denotes statistical significance, and the x-axis shows the combined score. (B) Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment map of the top significantly enriched KEGG pathways in ITP vs healthy controls (all were upregulated). Edges indicate gene overlap, and node size reflects enrichment significance. (C) Gene Set Enrichment Analysis of platelet transcripts in ITP compared with healthy controls. Enrichment plots show pathway-specific enrichment scores across the ranked gene list. Positive enrichment scores indicate enrichment in ITP, whereas negative scores indicate enrichment in healthy controls. Adj, adjusted; ES, enrichment score; FDR, false discovery rate; NES, normalized enrichment score; q-val, q-value.

activation signature across all annotation frameworks (Figure 3A, B). The top enriched categories involved *Platelet activation, signaling and aggregation* (adjusted $P = 4.25 \times 10^{-21}$) and *Hemostasis* (adjusted $P = 1.11 \times 10^{-17}$). Upregulated transcripts included key components of integrin-associated signaling (*AKT1*, *FERMT3*, *ITGA2B*, *ITGB3*, *SRC*, and *TLN1*), as well as multiple genes involved in calcium-dependent signal transduction (*ATP2A3*, *CALM1*, *ITPR1*, *ITPR2*, *PRKCB*, and *SLC24A3*).

In addition to classical platelet signaling pathways, enrichment analysis highlighted categories annotated with immune- or pathogen-associated terms (*Immune System*, *Innate Immune System*, and *Infectious disease*), which showed substantial overlap with transcripts contributing to platelet activation and actin-dependent signaling processes.

In line with this platelet activation-related pattern, transcripts involved in cytoskeletal organization and adhesion, such as *ACTB*, *ARPC1B*, *FLNA*, *MAP1A*, *PARVB*, and *WASF2*, were significantly upregulated. Gene set enrichment analyses confirmed activation of Rho GTPase signaling and regulation of the actin cytoskeleton. In addition,

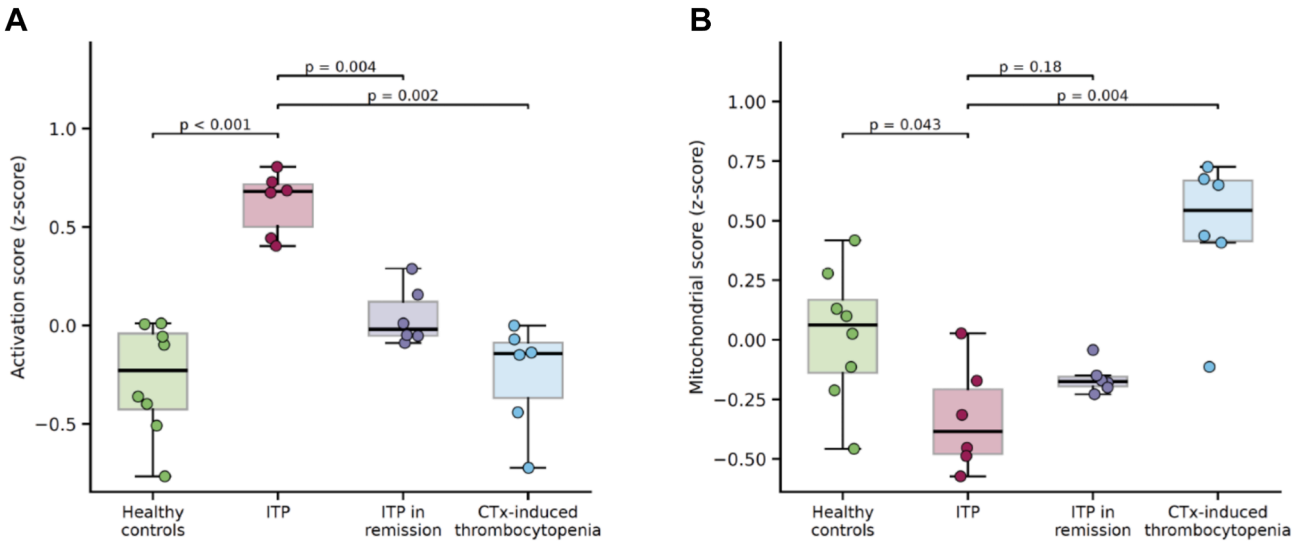


FIGURE 4 Group-level comparison of platelet activation and mitochondrial gene expression. Box plots of pathway expression scores from the different cohorts showing (A) the platelet activation signature, based on Kyoto Encyclopedia of Genes and Genomes (KEGG) "Platelet activation" (hsa04611), and (B) the mitochondrial oxidative phosphorylation (OXPHOS) and translation signature, based on KEGG "Oxidative Phosphorylation" (hsa00190) and Gene Ontology "Mitochondrial Translation" (GO:0032543). Per-sample scores were calculated from DESeq2-normalized counts ($\log_2$-fold–transformed and z-scored per gene). *P* values from 2-sided Mann–Whitney U-tests are indicated. CTx, chemotherapy; ITP, immune thrombocytopenia.

pathways related to vesicle-mediated transport and intracellular trafficking (*Endocytosis*, *Lysosome*, and *Autophagy*) were similarly upregulated, as evidenced by increased transcript levels of *ACTG1*, *DNM2*, *NBEAL2*, *PPP1CA*, *PRKCA*, and *RHOA*.

At the same time, several transcripts associated with cytoskeletal organization and vesicle recycling were downregulated, including *PKN2*, *RAB11A*, *RASA1*, *RGS18*, *RHOBTB3*, *SLAIN2*, *TBC1D31*, and *TMSB4X*. This indicates selective, bidirectional transcript changes within vesicle- and cytoskeletal-associated pathways.

Reduced transcript levels were most prominent in mitochondrial and metabolic pathways. This included decreased RNA levels of several nuclear-encoded mitochondrial factors involved in RNA processing and translation (eg, *NDUFV2*, *NDUFS6*, *MRPS9*, *MRPS14*, *MRPL3*, *ATP5ME*, and *ATP5MK*), as well as lower abundance of all mitochondrially encoded RNAs in ITP than in healthy controls.

The observed patterns were further supported by gene set enrichment analysis of the ranked transcriptome (Figure 3C).

In addition to protein-coding transcripts, RNA sequencing captured multiple classes of noncoding RNAs. Across samples, more than 4000 annotated long non-coding RNA (lncRNA) loci were detected, with a subset showing differential transcript abundance between ITP and control platelets, including the most significantly altered lncRNAs: *C6orf223*, *ZNF346-IT1*, *DLGAP1-AS2*, *MAP3K14-AS1*, and *SCIRT*. Small RNA species were also detected, including several microRNAs, small nuclear RNAs, and small nucleolar RNAs, some of which showed significantly different expression between ITP and controls. However, because ribosomal RNA (rRNA) depletion protocols are suboptimal for small RNA recovery, these data do not permit reliable quantitative assessment.

3.3 | Comparison with chemotherapy-induced thrombocytopenia suggests ITP-specific signatures beyond those of regenerative thrombocytopenia

To determine whether the transcriptional changes observed in active ITP platelets are disease-specific or reflect more general regenerative features of thrombocytopenia, we compared platelet transcriptomes from patients with ITP with those from individuals with chemotherapy-induced thrombocytopenia. The chemotherapy-induced thrombocytopenia cohort comprised patients with acute myeloid or lymphoid leukemia in documented complete remission who were undergoing marrow recovery after consolidation chemotherapy. These patients had experienced profound chemotherapy-induced thrombocytopenia (nadir $< 10 \times 10^9$/L) followed by physiological platelet regeneration without evidence of persistent marrow damage or immune-mediated platelet destruction.

Both ITP and chemotherapy-induced thrombocytopenia were associated with increased RNA yield relative to blood PLT, consistent with enrichment of RNA-rich young platelets in both thrombocytopenic conditions. In line with this, both ITP and postchemotherapy platelets showed increased abundance of transcripts associated with vesicle-mediated transport and membrane trafficking, with significant enrichment of categories, including *Endocytosis* (KEGG) and *Membrane trafficking* and *Vesicle-mediated transport* (Reactome). However, a robust and coordinated platelet activation signature at the pathway level was observed only in ITP. The Reactome term *Platelet activation, signaling and aggregation*, which ranked among the most enriched categories in ITP, was not enriched in chemotherapy-induced thrombocytopenia; moreover, the KEGG *Platelet activation* pathway was significantly reduced in postchemotherapy samples compared with

healthy controls (adjusted $P = 7.3 \times 10^{-4}$). Thus, coordinated activation-related transcriptional changes were specific to ITP, whereas chemotherapy-induced thrombocytopenia did not show enrichment for platelet activation pathways (Figure 4A).

While both thrombocytopenic conditions showed a similarly reduced abundance of mitochondrially encoded RNAs, the nuclear-encoded mitochondrial biogenesis program (oxidative phosphorylation (OXPHOS) subunits and mitochondrial ribosomal proteins) was reduced specifically in active ITP and, conversely, elevated in chemotherapy-induced thrombocytopenia (Figure 4B).

3.4 | Attenuated activation-related transcriptional changes in ITP in treatment-free remission

To assess whether the transcriptional profile of active ITP normalizes with restoration of PLT, platelet transcriptomes from ITP patients in treatment-free remission were analyzed. In platelets from remission samples, substantially fewer transcriptional differences relative to healthy controls were observed (1093 DEGs vs controls; 6985 DEGs in active ITP). In particular, the strongly coordinated activation-related transcriptional signature observed in active ITP was largely attenuated. A subset of activation-related transcripts nevertheless remained elevated in remission compared with healthy controls, including the $\alpha_{IIb}\beta_3$ integrin components *ITGA2B* and *ITGB3*, as well as selected calcium-signaling and cytoskeletal transcripts, while phosphoinositide 3-kinase (PI3K)/mitogen-activated protein kinase (MAPK) signaling components and α-granule secretion markers returned to control levels. Overall, remission samples showed expression profiles intermediate between active ITP and controls, with greater intersample variability (Supplementary Figure S2). In remission samples, expression profiles tended to vary with the degree of platelet recovery: samples from patients with PLT $< 150 \times 10^9$/L more closely resembled active ITP and showed a more pronounced activation-related pathway profile (Supplementary Figure S3).

4 | DISCUSSION

This study provides, to our knowledge, the first transcriptome-wide RNA sequencing analysis of highly purified platelets from patients with active primary ITP. Despite profound thrombocytopenia, all samples yielded high-quality RNA sequencing data, demonstrating the feasibility of platelet transcriptomic profiling even at very low PLT. Platelets from patients with active ITP displayed a distinct RNA profile characterized by convergent upregulation of activation-related pathways across all annotation frameworks. Many of these activation-associated transcripts overlap with known markers of young RNA-rich platelets, indicating that part of the observed variation reflects compositional differences in platelet age, specifically, an increased proportion of reticulated platelets. However, the magnitude and pathway coherence of the activation signature exceed patterns typically attributable to this immature platelet population [30,31], supporting a contribution from disease-specific factors beyond compositional shifts. The comparison with chemotherapy-induced thrombocytopenia provides additional support for the disease specificity of these findings. Despite similar increases in RNA yield and cytoskeletal- and adhesion-related transcripts in both groups, only platelets from active ITP displayed a coordinated activation-related transcriptional program, whereas some canonical activation pathways were not enriched and, in some cases, even reduced in chemotherapy-induced thrombocytopenia. This indicates that disease-associated factors in ITP, rather than mere regenerative thrombopoiesis, may contribute to an activation-primed platelet state, consistent with prior functional studies demonstrating platelet hyperreactivity in ITP [32,33].

As for the immune-related pathway categories enriched in ITP platelets, many of the contributing transcripts have established dual roles in platelet activation and immune signaling, and the immune-related enrichment in our data is therefore not fully separable from the activation signature. The activated phenotype of ITP platelets may itself contribute to the maintenance of immune dysregulation. However, direct evidence for such a contribution or active immunoregulation by platelets cannot be derived from our transcriptomic data alone and requires functional studies of platelet-immune cell interactions.

In addition to the activation-related changes, ITP platelets showed a broad reduction in transcripts encoding mitochondrial and metabolic functions. This included multiple nuclear-encoded mitochondrial genes involved in RNA processing and mitochondrial dynamics, as well as mitochondrially encoded RNAs. Such concordant depletion of mitochondrial transcripts may indicate altered mitochondrial function in ITP platelets, consistent with prior reports describing mitochondrial depolarization, increased oxidative stress, and enhanced susceptibility to apoptosis [34–37].

When interpreting the results of this study, several biological and technical factors should be considered. The most important limitation is the absence of functional or proteomic validation, which was beyond the scope of this study. Since RNA abundance does not directly equate to functional activity, the findings require experimental validation in future studies.

A further consideration is that the platelet transcriptome is physiologically dynamic and varies with platelet age and maturity, even in healthy individuals [38]. A major interpretational challenge in platelet transcriptomics is therefore distinguishing disease-associated transcriptional changes from shifts in platelet population composition, since even in purified platelet preparations, heterogeneity in platelet age and RNA content can substantially influence global transcript profiles [39]. To address this, chemotherapy-induced thrombocytopenia was included as a nonimmune comparator with a comparable degree of thrombocytopenia and ongoing regenerative thrombopoiesis. This is, of course, not an ideal control condition, as cytotoxic therapy may specifically alter megakaryocyte gene expression, thereby introducing confounding transcriptional changes, consistent with the more pronounced separation of these samples in the PCA. Furthermore, parameters reflecting platelet maturity, such as the immature platelet fraction, may provide a more refined basis

for comparison than PLT in future studies. In addition, the inclusion of other regenerative or non-ITP conditions, such as posthemorrhagic thrombocytopenia or congenital thrombocytopenia, may further strengthen this approach.

A related question is at which level the observed transcriptional changes originate and by what mechanisms they are driven. Given that platelet RNA is largely inherited from megakaryocytes, disease-related alterations in megakaryopoiesis are likely to cause, or at least contribute to, the observed transcriptional landscape. In addition, circulating platelets may undergo further transcriptomic modulation upon exposure to autoantibodies or immune effector cells, particularly affecting mitochondrial and stress-responsive genes. Because bulk RNA sequencing captures averaged transcriptional profiles, the samples analyzed represent composite molecular signatures that cannot be resolved at the level of individual platelet subpopulations. Future studies integrating single-platelet transcriptomics with megakaryocyte analyses may help address this issue [40].

Furthermore, the modest sample size limits the statistical power to detect subtle transcriptional changes and may accentuate apparent differences, particularly given the known clinical heterogeneity of ITP. Although the present analysis was restricted to adult patients with primary ITP to reduce clinical heterogeneity, our cohort still included different disease phases, and patients in remission had received varied prior treatments. Transcriptomic patterns may also differ in pediatric or secondary forms of ITP, which were not addressed here. The predefined inclusion criterion of PLT $> 20 \times 10^9$/L precluded analysis of patients with more severe thrombocytopenia. Independent cohort validation will therefore be needed to confirm and extend these findings.

Given these limitations, this study identifies an ITP-specific platelet transcriptomic signature characterized by enrichment in activation-related pathways and downregulation of mitochondrial gene expression. This profile is consistent with previously described functional characteristics of platelets in ITP, including platelet hyperreactivity [3,33] and procoagulant platelet phenotypes [41–43]. These features are particularly interesting in the clinical context of ITP, as many patients exhibit only mild bleeding symptoms despite profound thrombocytopenia [44].

Collectively, these findings highlight both the feasibility and the interpretational complexity of platelet RNA sequencing and provide molecular support for the concept that platelets may reflect, and potentially contribute to, the immune and hemostatic landscape of ITP.

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AUTHOR CONTRIBUTIONS

J.-A.G., M.H., and U.A.F. performed data acquisition and analysis. K.T.-G. and C.T. supervised the study. J.-A.G. drafted the manuscript. All authors contributed to data interpretation, critically revised the manuscript, and approved the final version.

DECLARATION OF COMPETING INTERESTS

There are no competing interests to disclose.

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SUPPLEMENTARY MATERIAL

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