Klinikum rechts der Isar der Technischen Universität München
Department of Otorhinolaryngology

Role of platelets in tumor immune modulation via horizontal RNA transfer

Michael Siegl, Marie Kristin Fritsche, Tobias Weiser and Barbara Wollenberg

Introduction

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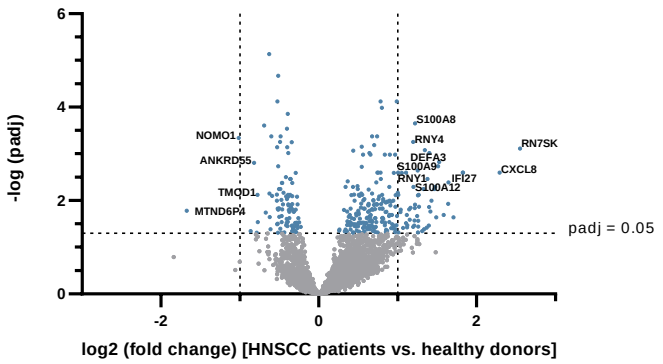

Fig. 1: Volcano plot showing the **differential expression analysis** (padj < 0.05) of platelet RNA from **55 HNSCC patients** and **17 healthy individuals**. In total we found 56 transcripts that were at least twice as abundant in HNSCC patients as in the healthy group.

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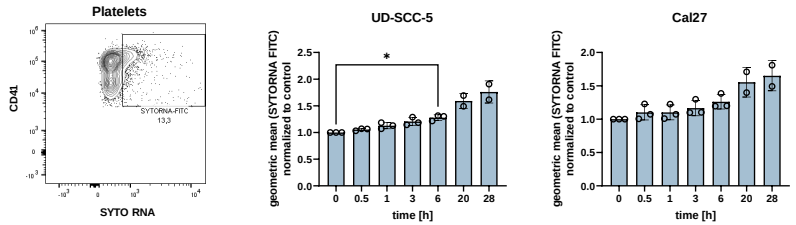

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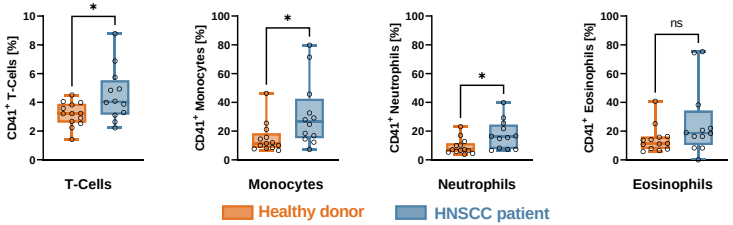

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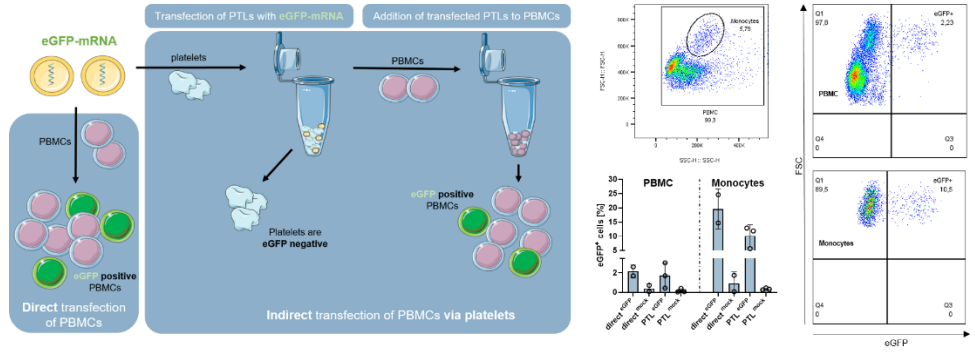

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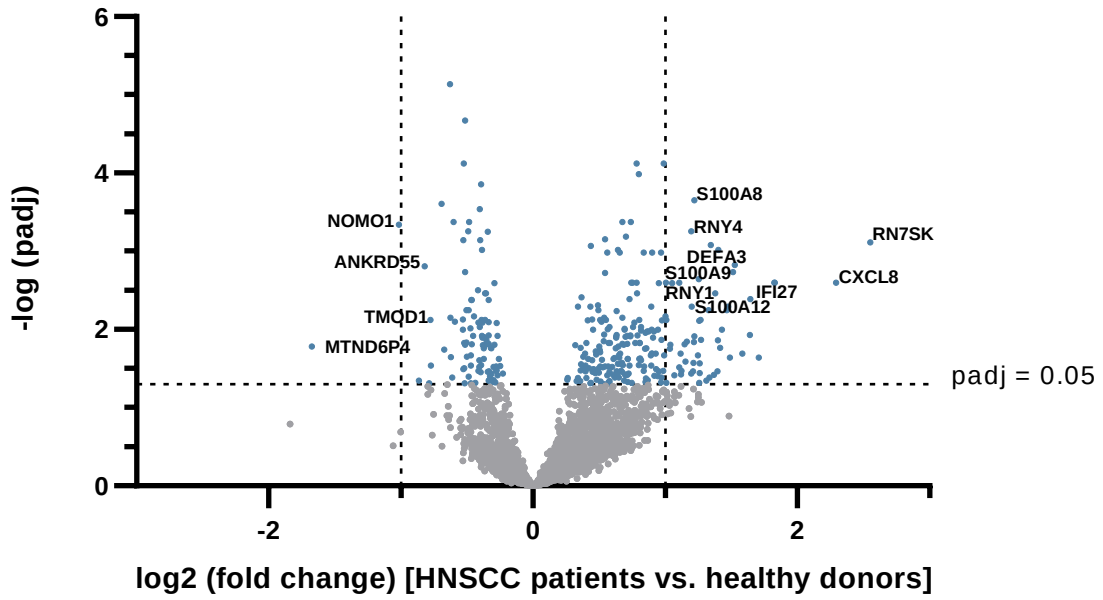

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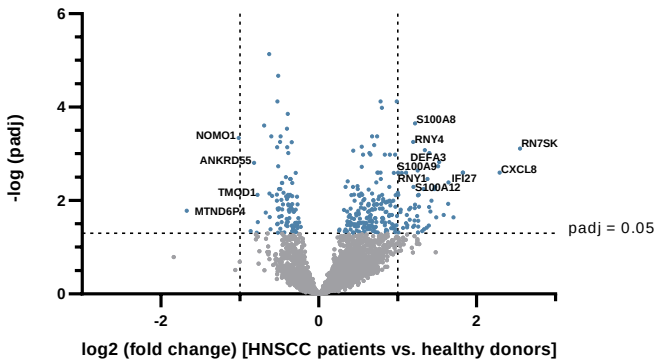

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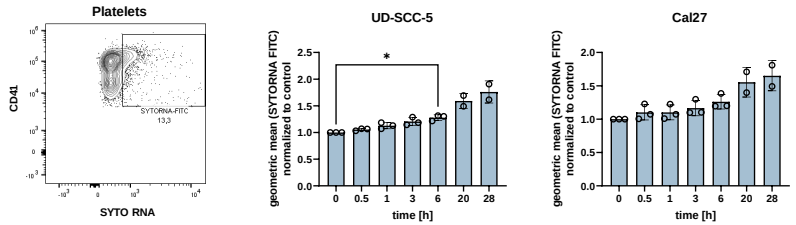

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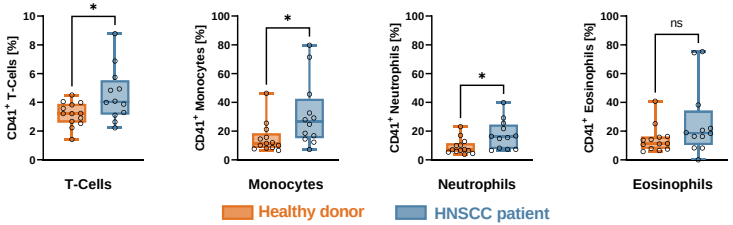

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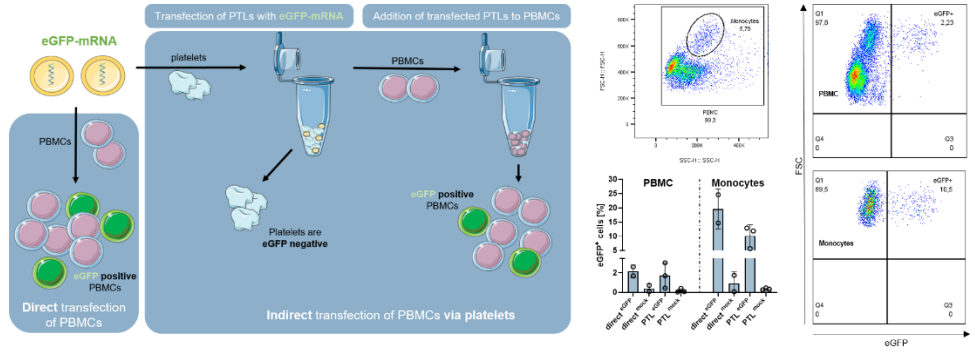

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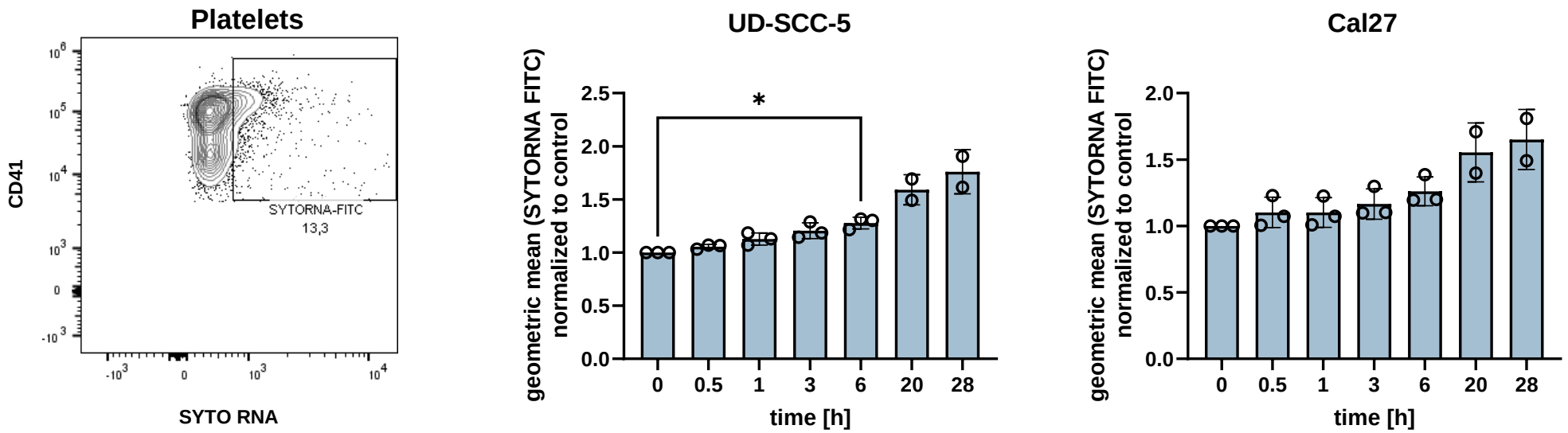

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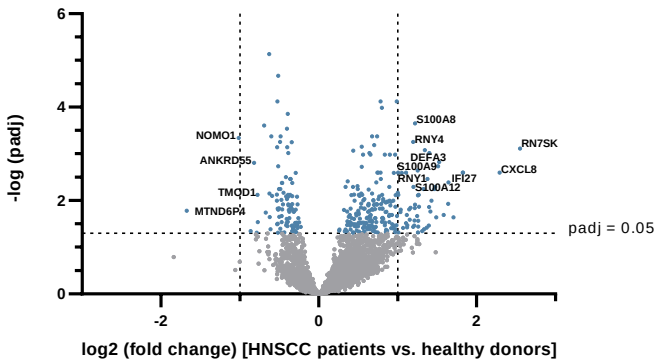

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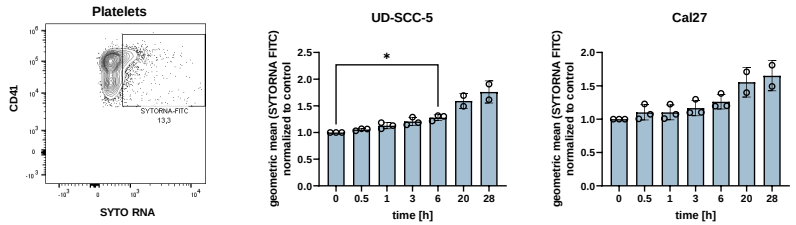

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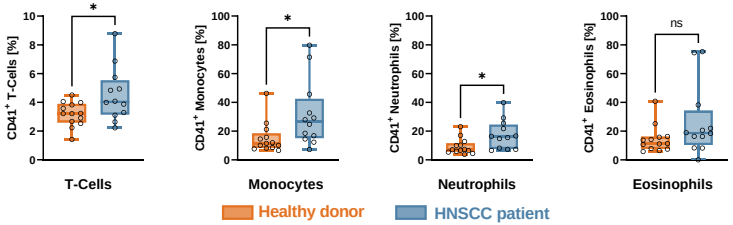

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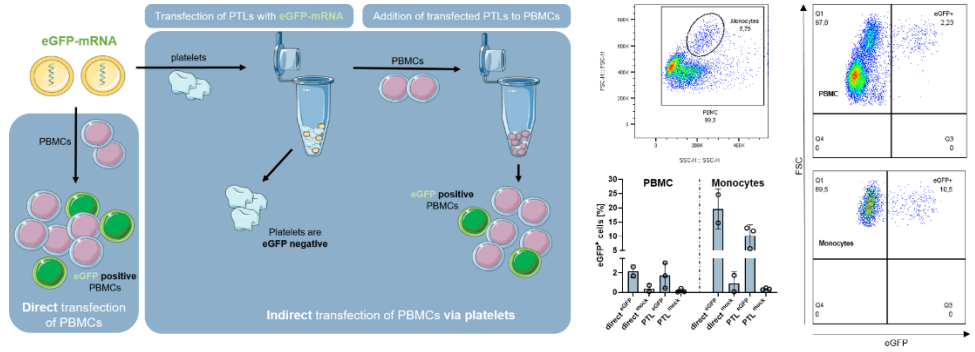

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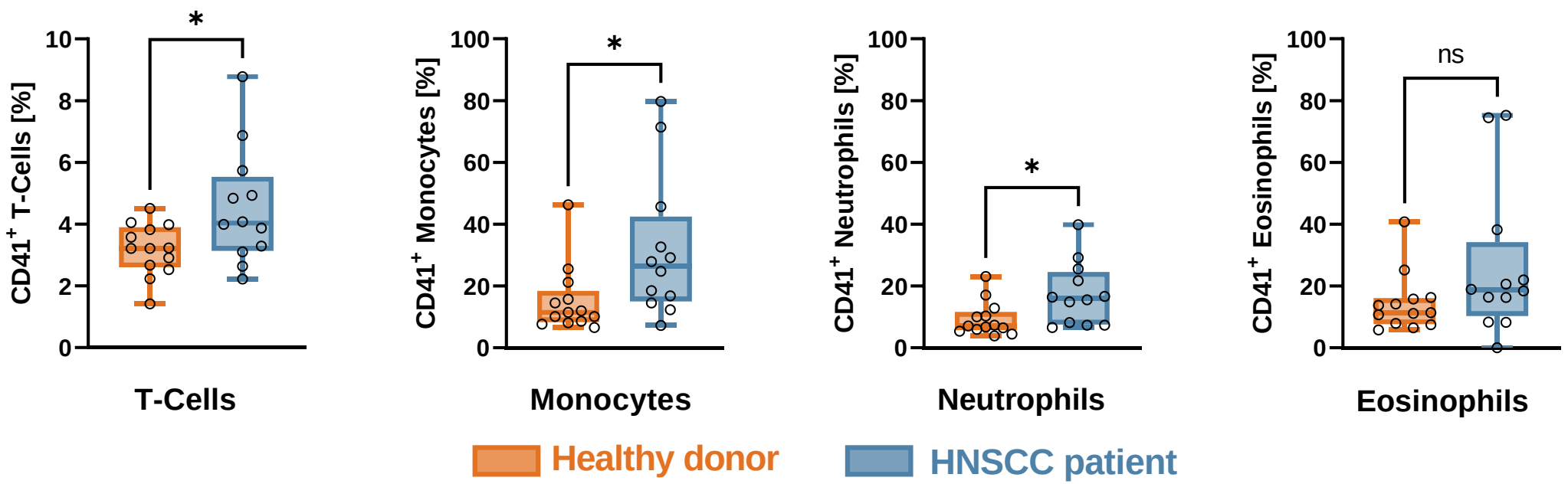

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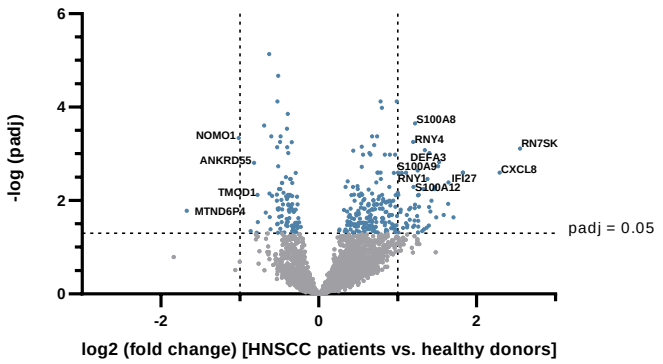

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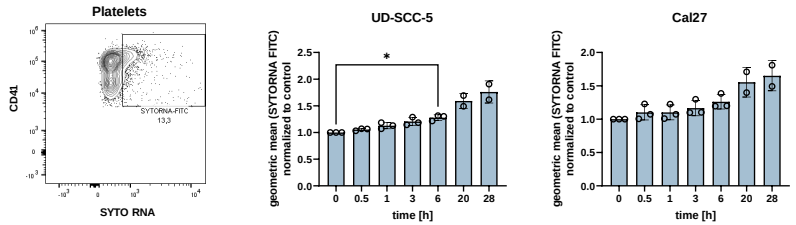

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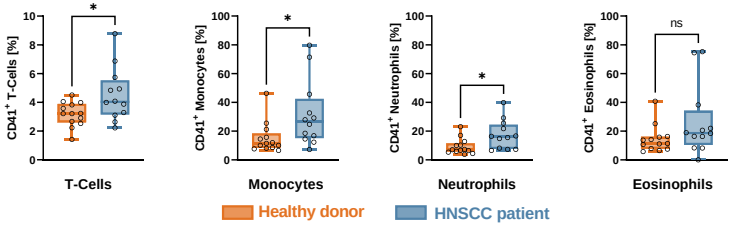

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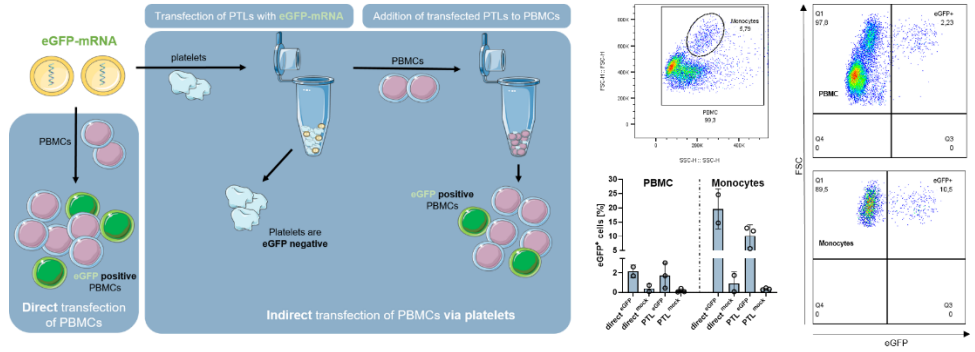

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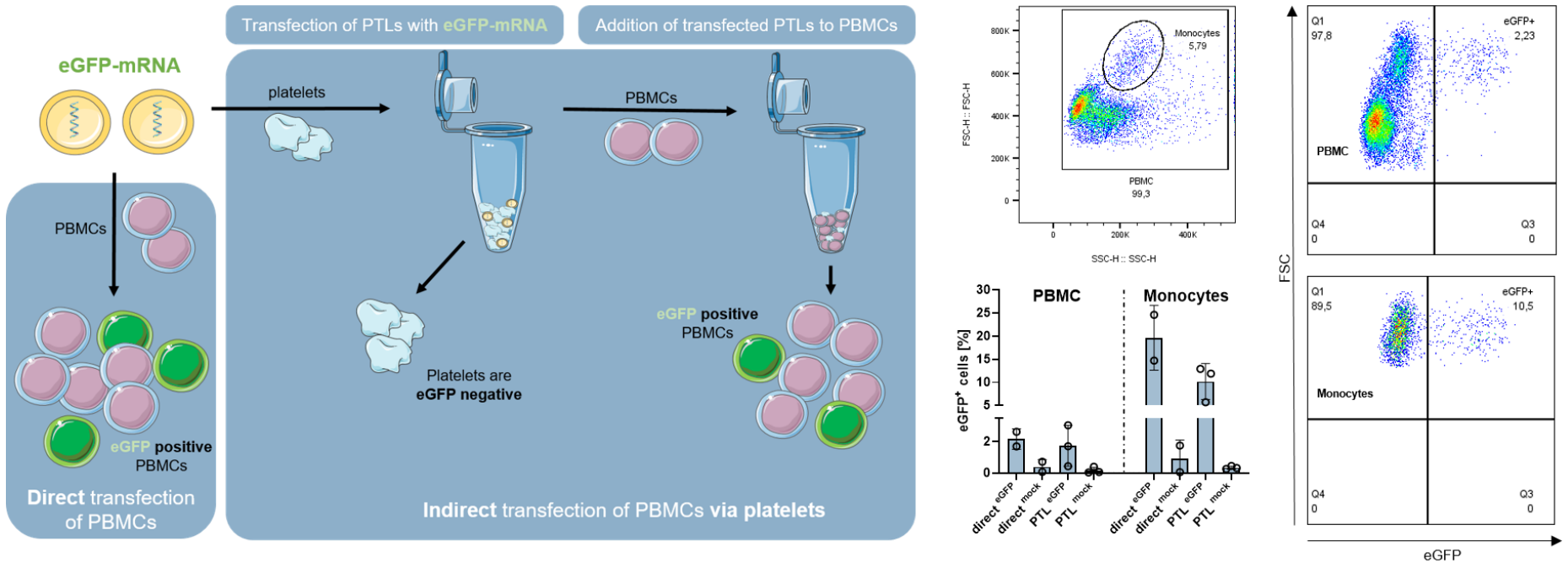

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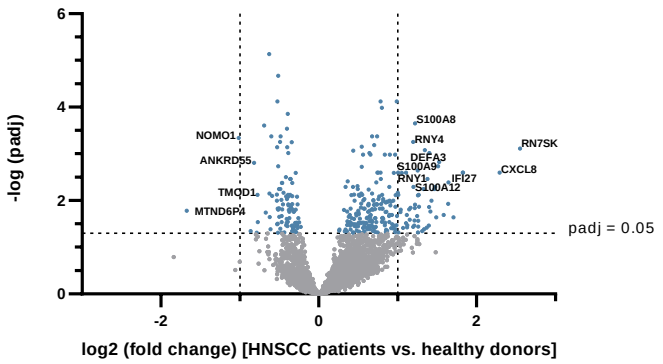

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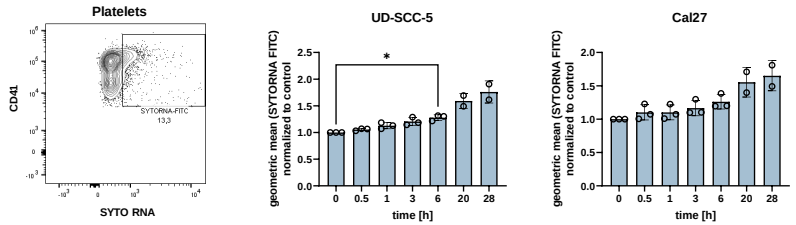

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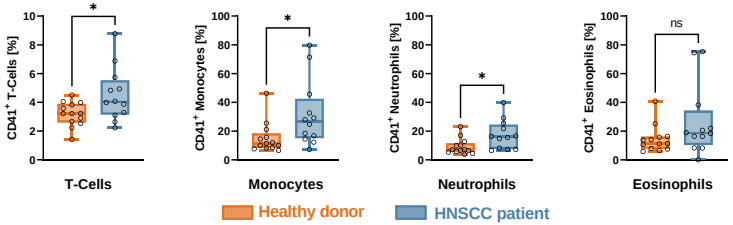

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4. Functional RNA transfer from platelets to PBMCs

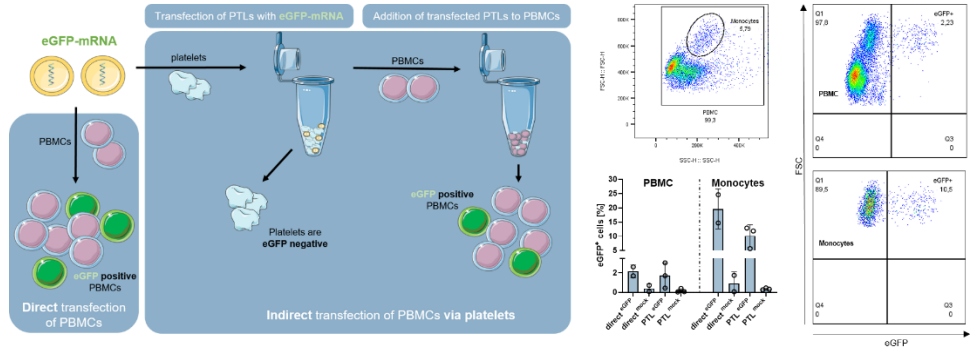

Fig. 4: To study the potentially functional transfer of RNA from platelets to recipient cells, platelets were transfected with mRNA coding for eGFP. After a washing step, those transfected platelets were co-incubated with isolated PBMCs for 24 hours (PTL ^{eGFP}). As control, PBMCs were also transfected directly with mRNA for eGFP (direct ^{eGFP}). On average, **transfection resulted in a fraction of 2.1% and 1.7 % eGFP-positive cells for direct or indirect transfection, respectively**. With respect to the subpopulation of monocytes, the eGFP-positive fraction was even more pronounced with 19.7% and 10.2% for direct and indirect transfection. Importantly, transfected platelets alone did not show eGFP expression (data not shown), **indicating a transfer of functional mRNA and not eGFP protein.**

Conclusion

Platelets of HNSCC patients do show a differential RNA profile compared to healthy individuals (Fig. 1). The presented data points to a direct transfer of RNA from cancer cells to platelets, which could contribute to this finding (Fig. 2).
Platelets not only are recipient of mRNA but also are able to pass it on to other cells, where it is actually used for protein synthesis. This could be shown especially for monocytes (Fig. 4).
Given the enriched leukocyte-platelet aggregates in HNSCC patients (Fig. 3), this might implicate a role of platelets in tumor immune modulation via horizontal RNA transfer.

Contact

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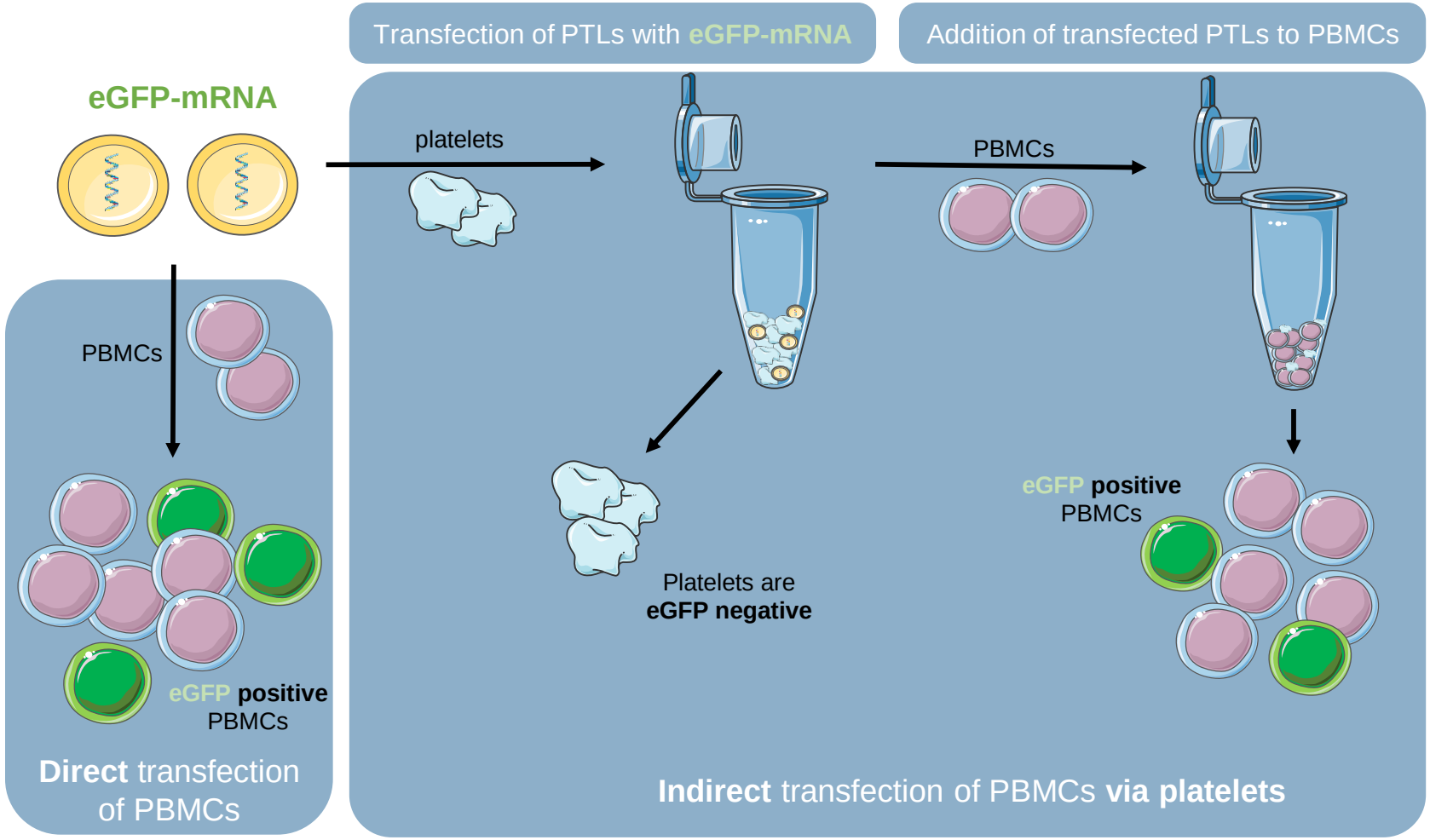
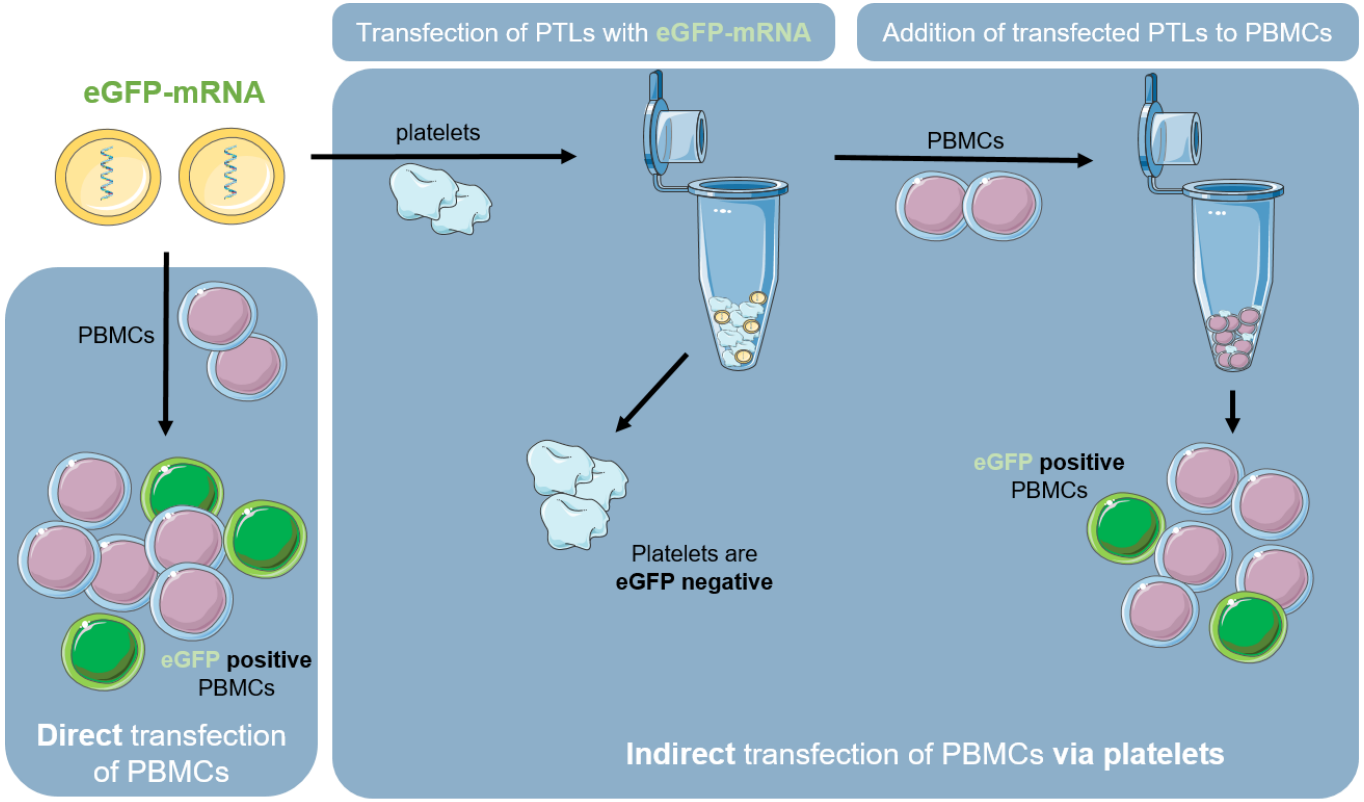
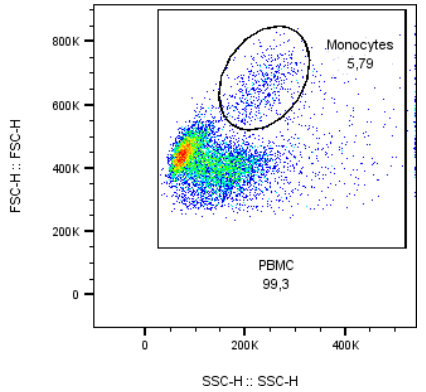
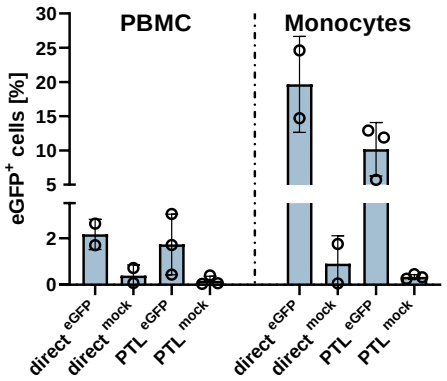
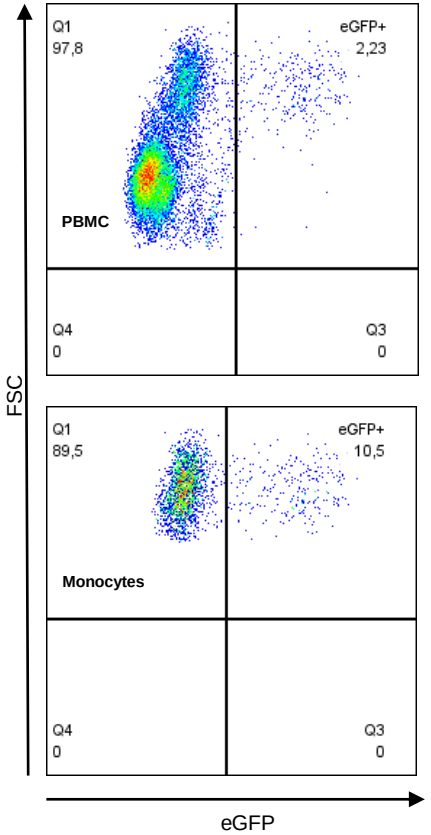

Transfection of PTLs with eGFP-mRNA
Addition of transfected PTLs to PBMCs
eGFP-mRNA
platelets
PBMCs
PBMCs
eGFP positive
PBMCs
Platelets are
eGFP negative
eGFP positive
PBMCs
Direct transfection
of PBMCs
Indirect transfection of PBMCs via platelets


Transfection of PTLs with eGFP-mRNA
Addition of transfected PTLs to PBMCs
eGFP-mRNA
PBMCs
eGFP positive
PBMCs
Direct transfection
of PBMCs
platelets
Platelets are
eGFP negative
PBMCs
eGFP positive
PBMCs
Indirect transfection of PBMCs via platelets


Monocytes
5,79
PBMC
99,3
FSC-H :: FSC-H
SSC-H :: SSC-H
800K
600K
400K
200K
0
200K
400K


PBMC
Monocytes
eGFP+ cells [%]
30
25
20
15
10
5
2
0
direct eGFP
direct mock
PTL eGFP
PTL mock
direct eGFP
direct mock
PTL eGFP
PTL mock


Q1
97,8
eGFP+
2,23
PBMC
Q4
0
Q3
0
Q1
89,5
eGFP+
10,5
Monocytes
Q4
0
Q3
0
FSC
eGFP