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An immune signature of postoperative cognitive dysfunction (POCD),a prospective cohort study

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Position du problème et objectif(s) de l'étude:
Post-operative cognitive decline (POCD) is one of the most common postoperative complications in elderly patients undergoing major surgery. While emerging preclinical evidence suggests that the systemic immune response to surgical trauma is a key pathobiological process driving POCD, studiesin patients are critically lacking (1).

Matériel et méthodes:
Blood samples from 33 elderly patients undergoing major orthopedic surgery - for whom the postoperative cognitive status was evaluated - were collected over four timepoints before and after surgery (day of surgery (DOS) and postoperative days (POD) 1, 7, and 90). They were analyzed using a combination of single-cell mass cytometry and plasma proteomics. We employed unsupervised clustering from correlation networks and univariate analyses to characterize the trajectory of immune cell distribution and signaling responses in patients with or without POCD. A stacked generalization (SG) predictive modeling approach was applied to classify patients at risk for POCD before surgery (2).

Résultats & Discussion:
Unsupervised analysis of the high-dimensional immunological data collected before and after surgery identified cell type and signaling-specific immune trajectories differentiating patients with and without POCD (Figure 1). Examination of the most prominent trajectory features revealed early exacerbation of JAK/STAT and dampening of IκB and NF-κB immune signaling responses to surgery in patients with POCD. Further analyses integrating immune cell responses, proteomic, and clinical data collected before surgery identified a robust predictive SG model that classified patients with and without POCD with excellent accuracy (AUC = 0.86, p = 2.2e-03).

Conclusion:
The single-cell immune system analysis of elderly patients undergoing surgery identified immunological trajectories differentiating patients with and without POCD, revealing a peripheral immune signature of POCD. In addition, a pre operative multi-omicmodel accurately predicted the later development of POCD, providing a promising strategy for future development of a diagnostic test for POCD guiding the individualized care of surgical patients.

Références bibliographiques:
(1) Hu, J. et al. Interleukin-6 is both necessary and sufficient to produce perioperative neurocognitive disorder in mice. Br J Anaesth (2018) (2) Rumer, K. K. et al. Integrated Single-Cell and Plasma Proteomic Modeling to Predict Surgical Site Complications. Ann Surg (2021)

Variable	β	95%CI	Score pondéré
IMC < 25 kg/m²	0.39	[0.13-0.66]	7
Redux	0.56	[0.07-1.04]	10
TP < 60 %	0.65	[0.19-1.09]	11
TCA > 1.2	0.36	[0.03-0.69]	6
Plaquettes < 150 G/L	0.56	[0.15-0.94]	10
Fibrinogène < 3 g/L	0.29_{ref}	[0.03-0.55]	5
Chirurgie combinée	0.59	[0.18-1.01]	10
Chirurgie aortique	0.45	[0.02-0.87]	8
Antiagrégant plaquettaire – simple*	0.40	[0.08-0.72]	7
Antiagrégant plaquettaire – double*	0.69	[0.14-1.22]	12

Tableau 3 : Variables préopératoire inclues dans le score POBS-CARD. Constant intercept β -2.15, modèle de régression logistique multivarié r^2=0.05 et Hosmer-Lemeshow 1.56, p=0.99.

* Traitement antiagrégant plaquettaire poursuivi jusqu'à la chirurgie

IMC : indice de masse corporelle ; TP : taux de prothrombine ; TCA : Taux de céphaline activé