3rd Meeting of the International Consensus Meeting
8-10 of May, 2025 Istanbul

Is there an immune proteome in PJI?

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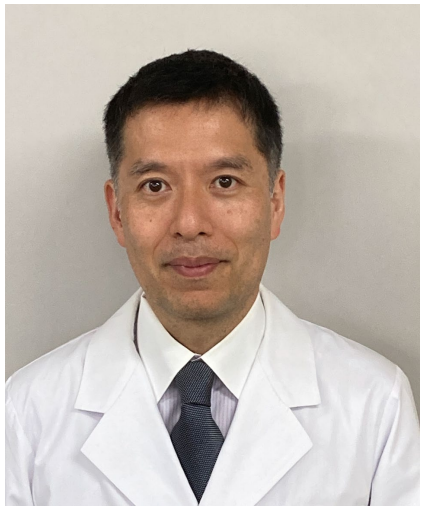
Kyle Cichos, USA


John Daiss, USA


Stephen Kates, USA


Gowrishankar Muthukrishnan, USA


Kohei Nishitani, Japan


Dina Raafat, Germany


Edward Schwarz, USA


Chao Xie, USA

Why is this topic Important

- PJI is a leading cause of arthroplasty failure– significant morbidity, mortality, cost
  - Substantial Host-related risk factors for PJI

- The role of the immune system in PJI gaining more attention
  - Immune proteome = collection of proteins including antibodies, cytokines, chemokines, and other immune cell signaling molecules, in response to an antigen challenge

- Technological advances and increased focus on the proteomic components in PJI have potential implications for improving:
  - Diagnostics: 20% culture negative – can we improve this?
  - Treatment: Role of immunotherapeutics to aid immune response and improve resolution?
  - Prevention: Potential for immune protein-based interventions to prevent PJI, such as vaccines

Literature Review/Process

- Number of articles retrieved: 533
- Screening: 129
- Final number of publications: 60
  - 29 drive majority of broad findings (beyond alpha-defensin, leukocyte esterase, and CRP)

Findings from Literature

Compartment	Synovial Fluid		Peripheral Blood/Serum	Local Tissue (synovium/bone)	Implant Sonicate Fluid
Technique	LC-MS	ELISA/Multiplex ASSAY	ELISA/Multiplex ASSAY	LCMS	LCMS
Increased^	MNDA**, PRTN3**, LTF***, LRG1, CRP, S100A8/A9, ANXA2, PRG4, CR-TAC1, LCN2, MPO, CTDG, MMP-9, PYGL, others	IL-1ra, IL-1a**, IL-1b******, IL-2, IL-4**, IL-5****, IL-6********, IL-8*******, IL-10****, IL-12, IL-17****, IL-19, IL-20, IL-22, IL-35, TNF-α****, INF-γ****, G-CSF**, GM-CSF, MIP-1a, MIP-1B**, MMP-1, MMP-2, MMP-3**, SKALP, FGF-basic, CCL20, OSM, EN-RAGE, LL-37, HBD-3, a2-macroglobin, b2-microglobin, VEGF, VCAM1, TNF-b, vWF, TIMP1, sTNF-R1, sTNF-R2, pentraxin-3, sCD163, sCD30, TSLP, APRIL, BAFF, GROA (CXCL1) Leukocyte esterase, alpha defensin, CRP, S100A8 (calprotectin) C1q, C3b/C3i, C4b, C5, C5a, MBL, properdin, LCN2	IL-4, IL-6****, IL-17, Ferritin, HBD-2, sTNF-R1, sTNF-R2, BAFF, APRIL, TSLP, pentraxin- 3, cfDNA, S100A8 (calprotectin), neutrophil elastase, DNaseI	C3, GGH, ORM2, ITGB2, ACTR2, MMP-9, MPO, ITGAM, HP, PRKCD, C4A, CTSG, PRTN3, HSP90AA1, CTSA, CYBB, RNASE3, SDCBP, LTF, others	S100A8/A9, LRG1, ANXA2, PRG4, CR-TAC1, LTF, LCN2, MPO, CTDG, MMP-9, PYGL, others
Decreased^		IL-5, RETN (ADSF); CSF-1, OPG, Flt3L, AXIN1, osteocalcin	TWEAK, osteocalcin; MMP-2, sIL-6Ra	PYGB, LAMB1, ITGB1, EGFR, CD59, others	
No Change^		IL-2*, IL-4, IL-6, IL-12p70, IL-13, IL-23, TNF-a, HBD-2, GM-CSF, glucose	IL-1a, IL-1b, IL-2, IL-8, G-CSF, TNF-a, LL-37, HBD-3		

^PJI vs Aseptic revision

Findings from Literature

- Multiple tissue compartments studied– sonicate fluid, synovial fluid, synovium, bone, peripheral blood, etc
  - Location variability
- Multiple techniques for studying and quantifying the immune proteome – variability in results
- Innovative technology and analysis platforms/methods continue to evolve our understanding
- Pathogen-specific humoral immune proteome
  - High antibody titers against an S. aureus heme-scavenging protein IsdB = increased adverse events postop
  - Antibodies against the glucosaminidase (Gmd) subunit of S. aureus autolysin (Atl) or high titers of Amd, CHIPS, SCIN, or Hla = decreased adverse events postop
- The immune proteome in PJI is currently targeted for improvement in diagnostics, prognostics, prevention, and treatment of PJI

Question:

- Is there an immune proteome in PJI?

Response:

- Yes, there is an immune proteome in PJI, and our understanding of this proteome continues to grow and evolve.

- Level of Evidence: Moderate

❖**Vote:**

Agree	**38; 100%**
Disagree	**0**
Abstain	**0**