PROMETHEUS: What Does It Do?

Project for Military Exposures and Toxin History Evaluation in U.S. Service Members

(DoD/USUHS Murtha Cancer Center)

Purpose & Aims

- Quantify cancer risk signals in U.S. military aviators (fixed- and rotary-wing aircrew & maintainers), focusing first on melanoma, prostate, and testicular germ cell tumors (TGCT).
- Identify pre-diagnostic biomarkers and exposure-response relationships using PROMETHEUS assets (DoDSR, JPC, ILER/VMOAT) and APOLLO workflows.
- Deliver actionable prevention, early detection, and precision-treatment insights that can translate to exposure-informed care in DoD/VA.

Target Population & Cohorts

- Active-duty, Guard/Reserve, and veteran aviators; comparison groups of matched non-aviator service members by age, sex, race/ethnicity, service, entry year, and duty station era.
- Sub-cohorts: fighter/attack, airlift/tanker, rotary-wing, trainers; maintainers (flightline, fuels, egress, avionics).

Primary Endpoints

- Incident cancers: melanoma, prostate, TGCT (primary); thyroid and non-Hodgkin lymphoma (secondary).
- Biomarkers: proteomic/metabolomic signatures, PFAS panels, inflammation/immune activation, DNA adduct surrogates; pathology features from JPC slides.
- Exposure metrics: ILER/VMOAT-derived exposures (JP-5/JP-8, AFFF/PFAS, solvents/degreasers, hydraulic fluids, hydrazine, EMF/radar, cosmic radiation proxies, cabin/cockpit air).

Study Design (PROMETHEUS/APOLLO-conformant)

1. Retrospective nested case-control using DoD Serum Repository (DoDSR) pre-diagnostic sera: identify aviator cases and matched non-aviator controls; perform multi-omics on archived sera; link to ILER/VMOAT exposure vectors and JPC pathology when available.
2. Prospective capillary blood biobanking using personally administered dried-blood microsampling (e.g., OneDraw) in aircrew and flightline maintainers: pre/post-sortie and pre/post-deployment sampling at participating MTFs; optional cockpit/flightline environmental sampling.
3. Data integration & analysis via Prometheus Data Platform (PDP) and Murtha Cancer Center Data Platform (MC2DP), interoperable with VA VPODC and NCI GDC/PDC/TCIA; analysis pipelines aligned to APOLLO.

Biospecimen Plan

- DoDSR: retrieve pre-diagnostic sera at T-3 to T-0 years before diagnosis; aliquots for proteomics, metabolomics, targeted PFAS and exposure panels.
- Prospective: 150 µL capillary blood (2×75 µL strips) per timepoint (DBS); optional venous plasma at select sites; serial sampling windows to capture acute/short-term exposure signatures.
- JPC: request digitized slides/tissue blocks for pathology features and spatial proteomics on selected cases.

- Environmental: flightline/cockpit passive samplers (PFAS precursors, VOCs, PAHs) at sentinel bases.

Data Joins & Covariates

- ILER + VMOAT: duty locations, MOS/AFSC, hazard records, deployment windows, TES annotations; derive exposure vectors and era‑/platform‑specific surrogates.
- Medical & outcomes: MHS GENESIS/CHCS, VA EHR, tumor registries, mortality, and service records; imaging via TCIA where available.
- Aviation‑specific: aircraft type, hours, sortie counts, night/AR refueling, squadron/BASOPS indicators (as available).

Analytics & Readouts

- Signal detection: conditional logistic regression, penalized models, and causal frameworks (targeted learning) for exposure‑cancer associations; multiple‑testing control.
- Multi‑omics: differential abundance, pathway enrichment, and proteogenomic signatures (APOLLO standard pipelines); pre‑diagnostic classifier development (ROC/AUC, calibration).
- Translation: risk‑stratified screening proposals (e.g., dermatologic surveillance cadence), exposure‑mitigation recommendations, and candidate precision‑therapy biomarkers.

Governance, Access & Compliance

- Sponsorship: MCCRP/APOLLO site PI with HJF regulatory support; IRB protocol leveraging PROMETHEUS framework (e.g., site '31B' precedents).
- Data security: PDP/MC2DP workspaces, Gen3‑based governance; de‑identification per DoD/VA policy; data‑sharing consistent with Cancer Moonshot principles.
- Regulatory: DoD HRPP/IRB, VA R&D where applicable; data‑use agreements for DoDSR/JPC/ILER.

Deliverables & Notional Timeline (first 12–18 months)

- Months 0–3: finalize PI/sponsor, protocol & IRB, PDP/MC2DP workspace creation; cohort definitions and pull lists (DoDSR/JPC).
- Months 4–9: retrospective biospecimen retrieval & assays; prospective pilot enrollment at ≥2 bases; initial exposure vectorization from ILER/VMOAT.
- Months 10–18: integrated analyses; interim readout to Cancer Cabinet‑aligned stakeholders; draft manuscripts and prevention/early‑detection proposals for aviators.

Key Interfaces / Points of Contact (indicative)

- MCCRP (USUHS) / PROMETHEUS Ops & Data teams; APOLLO site PIs; VA POP/VPODC liaisons; JPC consultation; AFHSD/DoDSR operations; ILER program office. This scheme aligns with PROMETHEUS scope (Moonshot 2.0), APOLLO workflows, DoDSR/JPC assets, ILER/VMOAT exposure linkage, and PDP/MC2DP data platforms.