Comprehensive Research Proposal: Personalized Medicine for Hypertension

1. Administrative Summary

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| Field | Detail |
| Title | Personalized Medicine Approach for Hypertension Management: A Multi-Omics Study in a High-Risk Cohort
Image of DNA double helix

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Department	Department of Cardiovascular Medicine
Field	Personalized Medicine, Cardiology, Pharmacogenomics
Project Start Date	2026-03-01
Project End Date	2029-02-28

2. Abstract (Maximum 300 words)

Hypertension affects billions globally, yet treatment efficacy is highly variable, leading to significant rates of resistant hypertension and subsequent cardiovascular events. Current prescribing practices rely on a 'one-size-fits-all' empirical approach. This project proposes a comprehensive, three-year, prospective multi-omics study to transition hypertension management toward a precision medicine paradigm. We will recruit 500 patients with newly diagnosed or treatment-naïve Stage II hypertension from high-risk demographics. Participants will undergo whole-exome sequencing, targeted metabolomics, and baseline clinical assessment. They will then be treated with standard first-line anti-hypertensive medications, with response monitored over 12 months. The multi-omics data will be integrated with clinical outcomes using advanced machine learning models to identify genetic and metabolic signatures that predict drug response (efficacy and adverse events). The primary objective is to develop a validated Personalized Treatment Algorithm (PTA) that guides the selection of the optimal anti-hypertensive agent based on an individual patient's molecular profile. This research is expected to significantly reduce treatment failure, minimize side effects, and optimize therapeutic outcomes, thereby lowering the public health burden of uncontrolled hypertension.

3. Project Objectives

1. **Biomarker Identification:** Identify specific genetic variants (via whole-exome sequencing) and metabolic markers (via metabolomics) that robustly correlate with differential response to three major classes of anti-hypertensive drugs (ACE inhibitors,

Calcium Channel Blockers, Diuretics).
2. **Algorithm Development:** Develop and refine a data-driven Personalized Treatment Algorithm (PTA) capable of accurately predicting the optimal initial drug therapy for a patient based on their pre-treatment multi-omics profile.
3. **Prospective Validation:** Conduct a small-scale, prospective clinical validation study comparing the efficacy of the PTA-guided treatment arm against the standard-of-care empirical treatment arm in a new cohort.

4. Methodology and Design

The study is designed as a three-year, hybrid prospective observational and interventional study.

Phase 1: Recruitment and Data Generation (Months 1–12)

- **Cohort:** Recruitment of 500 participants (age 35-75) with Stage II hypertension.
- **Baseline Data:** Collection of detailed clinical history, lifestyle factors, and blood samples.
- **Omics Data:** Whole-exome sequencing and targeted metabolomics performed on baseline blood samples.

Phase 2: Observational Treatment and Modeling (Months 6–24)

- Participants commence standard anti-hypertensive therapy per current guidelines (single-blinded to the research team).
- Clinical response (blood pressure reduction, side effects) is monitored quarterly for 12 months.
- Statistical analysis (GWAS, machine learning) is performed to correlate omics data with treatment outcomes, culminating in the Personalized Treatment Algorithm (PTA).

Phase 3: Algorithm Validation (Months 25–36)

- Recruitment of a new, independent cohort (N=100).
- **Randomization:** Cohort is randomized 1:1 into two arms:
  - **Algorithm Arm:** Drug therapy selection is guided by the PTA.
  - **Standard Arm:** Drug therapy selection follows current clinical guidelines.
- **Outcome:** Comparison of time-to-target blood pressure and rate of successful monotherapy between the two arms.

5. Project Timeline and Milestones

Milestone	Target Date	Deliverable/Description
M1: Protocol Finalization & Ethics Approval	2026-02-28	IRB approval secured and final protocol published.
M2: Cohort Recruitment Complete (N=500)	2027-02-28 (Month 12)	Completion of Phase 1 recruitment and baseline data collection.
M3: Omics Data Processing & QC Complete	2027-08-31 (Month 18)	Raw

sequencing/metabolomics data converted to usable, harmonized data sets. |
M4: PTA Algorithm Development	2028-06-30 (Month 28)	Finalized predictive model (PTA) and submission of first peer-reviewed manuscript.
M5: Validation Phase Complete	2029-01-31 (Month 35)	Completion of the prospective validation trial (Phase 3).
M6: Final Report and Data Archival	2029-02-28 (Month 36)	Submission of final grant report and deposition of all non-identifiable data/code to public repository.

6. Deliverables

1. **Personalized Treatment Algorithm (PTA):** A publicly available, open-source computational model (Python/R code) for predicting optimal anti-hypertensive drug response.
2. **Peer-Reviewed Publications:** Minimum of three high-impact publications detailing biomarker discovery, algorithm development, and clinical validation results.
3. **Curated Research Data:** Complete, anonymized multi-omics and clinical dataset archived in a recognized public repository (e.g., dbGaP).

7. Funding and Budget Summary

Funding Source	National Institutes of Health (NIH)
Funding Institution	The Global Health Research Foundation (Applicant Organization)
Grant Start Date	2026-03-01
Grant End Date	2029-02-28
Amount (Total)	$1,500,000
Breakdown (Year 1)	Personnel ($350,000), Supplies/Sequencing Costs ($100,000), Equipment/Computation ($50,000), Indirect Costs ($50,000).
Breakdown (Year 2)	Personnel ($370,000), Supplies/Metabolomics Costs ($120,000), Patient Incentives ($30,000), Indirect Costs ($50,000).
Breakdown (Year 3)	Personnel ($380,000), Publication Fees/Travel ($20,000), Validation Trial Costs ($50,000), Indirect Costs ($30,000).