

Biobanks Empower Personalized Treatment of Hypertension: Mechanism Exploration and Prospects

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Abstract. Recently, biobanks have significantly expanded in scale and functionality by systematically collecting diverse biological specimens, such as blood, urine, tissues, and DNA. This expansion provides crucial data support for precision medicine, particularly in disease diagnosis and treatment. As a highly prevalent chronic disease worldwide, hypertension presents limited efficacy with traditional therapeutic approaches due to its multifactorial pathogenesis. The deep integration of biobanks with hypertension research, however, is fostering a series of innovative pathways—by integrating multidimensional biological information from genomics, metabolomics, and other omics fields, combined with patients' clinical phenotypes and longitudinal follow-up data, individualized risk prediction models can be constructed to guide the selection of targeted drugs and optimize lifestyle intervention strategies. This data-driven precision medicine model provides a novel paradigm for addressing hypertension heterogeneity and establishes a scientific foundation for transitioning chronic disease management toward lifelong health stewardship.

Keywords: Biobank; Hypertension; Personalized Treatment; Digital Health.

1. Introduction

Hypertension occurs when blood pressure exerted by circulating blood on the arterial walls remains persistently elevated above normal levels. It is diagnosed based on repeated clinical measurements showing systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg. As one of the most common chronic diseases worldwide, hypertension often requires lifelong medication for most patients, leading to substantial economic burdens on households and considerable strain on public health systems. Surveys indicate that annual cardiovascular disease (CVD) care costs in low- and middle-income countries (LMICs) significantly surpass per capita health expenditures. This gap raises serious concerns about financial protection for CVD patients and, more generally, the sustainability of health financing systems [1-2].

Hypertension can be classified into three categories based on the magnitude of blood pressure elevation: Grade 1 (mild), Grade 2 (moderate), and Grade 3 (severe). Given the differential therapeutic requirements across these stages, personalized treatment strategies necessitate a patient-centric database to enable precision medicine. Empirical evidence consistently demonstrates that integrating biomarkers significantly enhances predictive accuracy while improving the sensitivity and specificity of identified patient subgroups.

This is how biobanks work in hypertension, particularly concerning the interplay between genetics and environmental factors. Firstly, genetic advancements are prominently demonstrated by identifying hypertension susceptibility loci using genome-wide association studies (GWAS) [3-5]. Notably, heterogeneity analyses have revealed critical findings: the rs11066015 variant in the ACAD10 gene exhibits significant sex-specific genetic effects on hypertension development, while the rs2074356 variant in the HECTD4 gene demonstrates pronounced genetic heterogeneity in systolic blood pressure regulation [6]. Second, gene-environment interactions are elucidated through salt-sensitivity biomarkers.[7]. These biomarkers integrate genetic variations with environmental exposure data, thereby elucidating the dynamic interplay between genes and environment in the pathogenesis of hypertension [8].

2. Current Studies

Biobanks are widely utilized in hypertension research. For example, Hussein Elghazaly et al. selected patients with clinically diagnosed hypertension or those prescribed antihypertensive medications (i.e., treated hypertension) based on primary care records, by examining variations in blood pressure control. Per guidelines from the National Institute for Health and Care Excellence (NICE), the following drug classes are classified as antihypertensive agents: angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), thiazide diuretics, α -adrenergic blockers, β -adrenergic blockers, and mineralocorticoid receptor antagonists (MRAs) [9-10].

2.1 Genomics and Pharmacogenomics Research Metabolomics

Genomics and pharmacogenomics research. Metabolomics, as a core branch of systems biology, systematically decodes the interactive effects between genetic background and environmental exposures (including diet, drugs, toxins, etc.) by quantitatively analyzing the dynamic changes of small-molecule metabolites within biological systems. This technology has been extensively integrated into the field of biomedical research, covering key directions such as biomarker discovery [11], elucidation of disease pathogenesis and drug activity [12], as well as investigations into drug-induced toxicity [13] and metabolic [14] pathways.

More specifically, pharmacometabolomics facilitates the identification of potential biomarkers for predicting individualized drug responses by detecting differential metabolites in pre-treatment baseline metabolic profiles and constructing correlation models between their variations and clinical outcomes. For instance, variations in the abundance of specific baseline metabolites can significantly distinguish patients' sensitivity or resistance to chemotherapeutic agents, thereby guiding the optimization of treatment regimens.

Meanwhile, metabolomics demonstrates distinct advantages in disease risk assessment. Integrating baseline metabolomic data from large-scale cohorts can establish quantitative association models between metabolic signatures and disease susceptibility. This metabolomics-based stratification strategy enhances the predictive accuracy of disease incidence and provides a scientific rationale for implementing precision prevention and patient stratification management [15].

Through empirical analysis, William R. Wikoff and colleagues demonstrated that atenolol-induced metabolomic profile alterations exhibit significant race and genotype-dependent variations. This study pioneered the establishment of a metabolomics-based framework for drug phenotypic analysis in hypertensive patients, elucidating the underlying molecular mechanisms driving racial disparities in therapeutic responses to atenolol. These findings provide critical theoretical insights for optimizing personalized medication strategies [16].

2.2 Multicenter Cohort Studies and Real-World Data Applications

The United Kingdom was at the forefront of establishing the biobank concept by launching the landmark UK Biobank project. Leveraging its massive sample size, comprehensive multidimensional data, and long-term follow-up tracking, this initiative has become an invaluable resource in global biomedical research. It has yielded substantial achievements in elucidating disease pathogenesis and exploring genetic-environmental interactions. Building on this platform, Shiyu Zhang et al. conducted a trajectory analysis using UK Biobank cohort data, employing multistate and mediation analysis methods to systematically investigate associations between air pollution exposure and dynamic disease progression from prehypertension (pre-HTN) to subsequent hypertension (HTN), cardiovascular disease (CVD), and death.

The study revealed statistically significant correlations between exposure to five air pollutants and CVD progression, with air pollution-induced CVD advancement potentially mediated partially by intermediate disease states in individuals. These findings suggest that strengthening preventive interventions for prehypertensive states could significantly reduce CVD progression risk. Future

research should further explore the driving mechanisms of air pollution in CVD development trajectories to provide a stronger scientific basis for healthcare policy formulation and intervention optimization [17].

China has launched large-scale population-based cohort studies, creating pivotal platforms for advancing hypertension etiology research and precision prevention through systematic data collection and long-term follow-up. Among these, the China Kadoorie Biobank (CKB) [18] and other representative projects have enrolled over 500,000 participants from diverse geographic regions and age groups, establishing a multidimensional health database that spans the entire lifespan. These initiatives adhere to standardized protocols for comprehensive data acquisition, including clinical information on hypertensive patients (e.g., blood pressure trajectories, comorbidities, medication histories), multi-omics biospecimens (blood, urine, tissue), environmental exposure data (diet, air pollution, occupational factors), and longitudinal follow-up outcomes (lifestyle patterns, disease progression, clinical endpoints). This integrated approach has resulted in a highly consolidated research repository.

By leveraging such resources, researchers can systematically investigate the complex interplay between genetic susceptibility, environmental modulators, and clinical phenotypes in hypertension pathogenesis, ultimately informing the development of tailored prevention strategies and evidence-based interventions.

Using these datasets, researchers can perform multilevel analyses: The first involves identifying genetic predispositions, with key genetic variants linked to hypertension risk (such as polymorphisms in *AGT*, *ACE*, and *ADD1*) discovered through genome-wide association studies (GWAS) and epigenomic analysis [19-20]. Gene-environment interactions are also crucial: By combining metabolomics and proteomics techniques, studies have clarified how environmental factors (like high-salt diets and obesity) interact with genetic backgrounds to influence blood pressure regulation through specific metabolic pathways, including the renin-angiotensin system (RAS) and oxidative stress responses. Pharmacogenomic evaluation also contributes: Analyzing correlations between long-term medication data (such as type, dose, and adherence to antihypertensive drugs) and clinical outcomes provides empirical evidence to assess racial differences in drug effectiveness, helping to improve personalized treatment plans.

These findings deepen scientific understanding of hypertension heterogeneity and establish a data-driven foundation for developing stratified prevention strategies and identifying novel therapeutic targets.

2.3 Standardization and Intelligent Management of Biobanks

In the wave of the significant data era, data privacy is confronted with ever more stringent demands, which concern the adherence to fundamental societal ethical standards and are intricately linked to realizing social equity. China has introduced the General Requirements for the Quality and Competence of Biobanks (GB/T 37864-2019), which provide detailed and comprehensive regulations on data privacy protection throughout the sample lifecycle, from collection and storage to use and destruction. This standard explicitly mandates that biobanks implement stringent information security management systems, utilize encryption technologies to safeguard data transmission and storage, and prevent data leakage or misuse. Meanwhile, it places significant emphasis on obtaining fully informed consent for sample utilization, thereby genuinely respecting individual rights and interests. Implementing this standard has significantly enhanced the standardization level of biobanks in China and contributed uniquely Chinese wisdom and viable solutions to global biobank data privacy protection, vigorously driving the industry towards healthy and orderly development [21-22].

3. Future Research Directions

3.1 Breakthrough Applications of Single-Cell Sequencing and Spatial Transcriptomics

In renal disease research, single-cell sequencing technology has demonstrated immense application potential, offering novel perspectives and methodologies for a deeper understanding of disease mechanisms. This technology holds particularly significant reference value in the study of hypertensive renal lesions.

Blue B Lake et al. investigated the adult human kidney using single-nucleus droplet-based RNA sequencing (snDrop-Seq) technology. They successfully resolved 30 distinct cell populations within the kidney and identified over ten molecular transition states between nephron regions in two major renal areas. More importantly, this study described genes with differential expression associated with chronic kidney disease, diabetes, and hypertension, providing crucial and vital reference evidence for research into the molecular mechanisms underlying hypertensive renal lesions [23].

Additionally, some research has focused on the microenvironment of early diabetic nephropathy using single-cell RNA sequencing technology. Although the research subject was diabetic nephropathy, the research methods and approaches are significant for studying hypertension-related tissues. This study revealed complex intercellular interactions and transcriptomic changes within the microenvironment. Specifically, by integrating receptor-ligand pairing resources, information on intercellular communication within the kidney is obtained. This achievement offers the possibility of understanding abnormal intercellular communication in hypertensive renal lesions [24].

Single-cell sequencing technology itself possesses numerous unique advantages. It can precisely detect rare cell types, uncover subtle differences between cell states, track cell developmental trajectories, and conduct in-depth analyses of intercellular interactions [25]. On the other hand, single-cell spatial sequencing technology enables the simultaneous acquisition of single-cell resolution and spatial information. This characteristic aids in a more profound understanding of the pathological mechanisms of hypertension [26].

In terms of technological integration, the research by Anna Maria Ranzoni et al. provides an excellent example. They employed single-cell RNA sequencing (scRNA-seq) and single-cell assay for transposase-accessible chromatin sequencing (scATAC-seq) technologies to analyze the differentiation trajectories of human fetal hematopoietic stem and progenitor cells. By integrating scRNA-seq and scATAC-seq data, they conducted in-depth research on hematopoietic stem cells' regulatory and transcriptional events [27]. This study demonstrates the feasibility of technological integration and offers clear ideas and a referable technical paradigm for integrating single-cell sequencing and spatial transcriptomics technologies.

3.2 Microbiome-host Interaction Studies

In relevant studies, fecal microbiota transplantation (FMT) experiments have revealed that FMT affects the integrity of the intestinal mucosal barrier. It suggests that blood pressure may be associated with butyrate-producing gut microbes and their functions regulating this barrier. This research provides experimental evidence for understanding the role of gut microbiota in the pathogenesis of hypertension, indicating that regulating the composition of gut microbiota may emerge as a novel therapeutic strategy for hypertension [28].

In fact, gut microbiota can modulate blood pressure through multiple mechanisms. On one hand, gut microbiota dysbiosis can trigger changes in host microbiota-related gene pathways, thereby influencing blood pressure. On the other hand, microbe-derived metabolites also exert significant impacts on blood pressure. For instance, short-chain fatty acids and indole-3-lactic acid benefit blood pressure, while trimethylamine N-oxide (TMAO) and other metabolites can have detrimental effects. Additionally, gut microbiota dysbiosis may disrupt the intestinal epithelial barrier, initiate systemic inflammatory responses, and activate traditional blood pressure regulatory mechanisms, such as the renin-angiotensin-aldosterone system, the autonomic nervous system, and the immune system.

Relevant reviews offer a comprehensive understanding of the complex relationship between gut microbiota and hypertension, highlighting the methodological and technical challenges that need to be addressed in future research [29]. Gut microbiota can regulate blood pressure by influencing various host systems, including metabolism, immunity, and the neuroendocrine system. Moreover, gut microbiota holds great potential as a new therapeutic target for hypertension. Adjusting gut microbiota composition through fecal microbiota transplantation, probiotic supplementation, and dietary modifications can improve blood pressure control. This provides a theoretical basis for gut microbiota regulation in hypertension and offers practical guidance, underscoring the pivotal role of gut microbiota in the pathogenesis and treatment of hypertension [30].

3.3 Deep Integration of Dynamic Health Data and Biobanks

In the context of the vigorous development of digital healthcare today, the deep integration of wearable devices and continuous monitoring technology demonstrates enormous potential. Advanced devices such as smart wristbands and blood pressure monitors [31], by virtue of their convenience and accuracy, can collect key physiological data from patients, including blood pressure, heart rate, and activity levels, in real-time and continuously [32]. Meanwhile, biobanks store patients' static genetic information, which contains the unique health codes of individuals. By organically integrating the dynamic data collected by wearable devices with the static genetic information in biobanks, comprehensive, detailed, and dynamically updated health profiles can be established for each patient, providing solid support for precision medicine [33].

4. Conclusion

Biobanks are expected to integrate further cutting-edge technologies, including single-cell sequencing, spatial transcriptomics, and microbiomics, to advance our understanding of the underlying pathological mechanisms of hypertension. Concurrently, through artificial intelligence-powered data analysis platforms, in-depth mining and clinical translation of cross-omics datasets will be achieved, facilitating breakthroughs in precision medicine and therapeutic development. This "data-driven" precision medicine model will reshape hypertension's diagnostic and therapeutic pathways and propel chronic disease management towards a lifelong health protection paradigm—from early disease warning to personalized interventions and post-recovery management, forming a closed-loop health management system. The collaborative innovation between biobanks and hypertension research injects robust impetus into humanity's endeavors to conquer chronic diseases and achieve the goal of healthy aging.

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