Ten Most Important Papers:

1. Khan AA, Agarwal H, Reddy SS, Arige V, Natarajan B, Gupta V, Kalyani A, Barthwal MK, **Mahapatra NR**. 2020. MicroRNA-27a is a key modulator of cholesterol biosynthesis. ***Mol Cell Biol*** 40:e00470-19.
2. Subramanian L, Maghajothi S, Singh M, Kesh K, Ananthamohan K, Sharma S, Khullar M, Victor SM, Swarnakar S, Asthana S, Mullasari AS, **Mahapatra NR**. 2019. A common tag nucleotide variant in *MMP7* promoter increases risk for hypertension via enhanced interactions with CREB (Cyclic AMP Response Element-Binding Protein) transcription factor. ***Hypertension*** 74:1448-1459.
3. Arige V, Agarwal A, Khan AA, Kalyani A, Natarajan B, Gupta V, Reddy SS, Barthwal MK, **Mahapatra NR**. 2019. Regulation of Monoamine Oxidase B Gene Expression: Key Roles for Transcription Factors Sp1, Egr1 and CREB, and microRNAs miR-300 and miR-1224. ***J Mol Biol*** 431:1127-1147.
4. Subramanian L, Khan AA, Allu PKR, Kiranmayi M, Sahu BS, Sharma S, Khullar M, Mullasari AS, **Mahapatra NR**. 2017. A haplotype variant of the human chromogranin A gene (CHGA) promoter increases CHGA expression and the risk for cardiometabolic disorders. ***J Biol Chem*** 292:13970-13985.
5. Gupta V, Kapopara PR, Khan AA, Arige V, Subramanian L, Sonawane PJ, Sasi BK, **Mahapatra NR**. 2017. Functional promoter polymorphisms direct the expression of cystathionine gamma-lyase gene in mouse models of essential hypertension. ***J Mol Cell Cardiol*** 102: 61-73. (***Cover page article***).
6. Kiranmayi M, Chirasani VR, Allu PK, Subramanian L, Martelli EE, Sahu BS, Vishnuprabu D, Kumaragurubaran R, Sharma S, Bodhini D, Dixit M, Munirajan AK, Khullar M, Radha V, Mohan V, Mullasari AS, Naga Prasad SV, Senapati S, **Mahapatra NR**. 2016. Catestatin Gly364Ser variant alters systemic blood pressure and the risk for hypertension in human populations via endothelial nitric oxide pathway. ***Hypertension*** 68:334-347.
7. Kalyani A, Sonawane PJ, Khan AA, Subramanian L, Ehret GB, Mullasari AS, **Mahapatra NR**. 2015. Post-transcriptional Regulation of Renalase Gene by miR-29 and miR-146 MicroRNAs: Implications for Cardio-metabolic Disorders. ***J Mol Biol*** 427: 2629–2646
8. Allu PK, Chirasani VR, Ghosh D, Mani A, Bera AK, Maji SK, Senapati S, Mullasari AS, **Mahapatra NR**. 2014. Naturally-occurring variants of the dysglycemic peptide pancreastatin: differential potencies for multiple cellular functions and structure-function correlation. ***J Biol Chem*** 289: 4455–4469.
9. SahuBS, Obbineni JM, Sahu G, Allu PKR, Subramanian L, Sonawane PJ, Singh PK, SasiBK, Senapati S, Maji SK, Bera AK, Gomathi BS, Mullasari AS, **Mahapatra NR**. 2012. Functional genetic variants of the catecholamine-release-inhibitory peptide catestatin in an Indian population: allele-specific effects on metabolic traits. ***J Biol Chem*** 287: 43840-43852***.***
10. SahuBS, Obbineni JM, Sahu G, Singh PK, Sonawane PJ, SasiBK, Allu PKR, Maji SK, Bera AK, Senapati S, **Mahapatra NR**. 2012. Molecular interactions of the physiological anti-hypertensive peptide catestatin with the neuronal nicotinic acetylcholine receptor. ***J Cell Sci*** 125: 2323–2337.

**Important discoveries/contributions as described in the above-mentioned papers:**

Cardiovascular diseases are the leading causes of morbidity/mortality worldwide. Although the mortalities associated with cardiovascular diseases are declining in high-income group countries (viz. Western Europe and North America) the burden of cardiovascular diseases continues to rise in the middle-income/ low-income group countries including India. Notably, South Asians have a greater prevalence of cardiovascular risk factors than the rest of the world, and India itself is estimated to have approximately half of the world’s heart disease patients. The determinants of cardiovascular diseases are multi-factorial, complex and often inter-related. Besides environmental factors (e.g., stress, inadequate physical activity, smoking, higher intake of fats and sodium, lower consumption of fruits and vegetables), a strong influence of genes in cardiovascular complications has been established. Genes involved in hypertension, dysregulated catecholamine homeostasis, dyslipidemia, increased oxidative stress, cardiac remodeling, protein misfolding are important regulators for cardiovascular/metabolic diseases. However, the pathogenesis of these diseases remains incompletely understood.

Dr. Nitish Mahapatra's research aimed at unravelling the genetic and molecular bases of cardiovascular diseases for their early diagnosis, prognosis and clinical management. He studied human subjects (cases versus controls), utilized rodent models (of hypertension, atherosclerosis and diabetes) as well as investigated at the cellular level (employing cultured cell lines) to elucidate how alterations in key genes/molecular factors contribute to disease phenotypes. Given below are his major scientific contributions:

**Discovery of functional genetic variations in Indian populations and their associations with cardiovascular/metabolic diseases**

He discovered a number of genetic variants in the chromogranin A gene that has emerged as new regulator of cardiovascular and metabolic diseases. Chromogranin A undergoes post-translational modifications and generates bioactive peptides such as anti-hypertensive/cardioprotective catestatin and dysglycemic pancreastatin. He undertook large scale case-control studies in Indian populations (using several thousand individuals from North and South India). Linkage disequilibrium analysis and genetic association studies identified several genetic variations in chromogranin A locus that enhance the risk for cardiovascular/metabolic disorders in Indian populations. Furthermore, using various experimental (cellular/ biochemical/ biophysical/ physiological assays), and computational (molecular modelling, molecular dynamic simulations, docking of peptides with their receptors) his research group demonstrated that these variants alter the expression of chromogranin A or potency of catestatin /pancreastatin peptides. Similarly, they have identified functional variants in the regulatory region of matrix metalloproteinases and established that these variants alter the risk factors for cardiometabolic disorders. These studies provided new molecular mechanisms contributing to cardiovascular diseases and have implications for development of diagnostic and therapeutic strategies for management of these diseases.

**Elucidation of mechanisms of differential expression of candidate genes of hypertension in rodent models**

His laboratory sequenced and compared the regulatory regions of various candidate genes implicated in cardiovascular diseases in inbred mouse models of genetic hypertension [viz., Blood Pressure High (BPH), Blood Pressure Normal (BPN) and Blood Pressure Low (BPL) animals]. Through this approach, they identified several novel polymorphisms which offered molecular insights into the genetic basis for the differential expression of candidate genes in these hypertensive models. For example, his research group discovered functional polymorphisms in the promoter region of HMG-CoA reductase (Hmgcr, the rate-limiting enzyme in the cholesterol biosynthesis pathway) and cystathionine gamma-lyase (Cth, a key enzyme involved in endogenous hydrogen sulfide production) genes that altered binding affinities of several transcription factors, such as n-Myc, Max, c-Fos (in the case of Hmgcr) and c-Rel, HOXA3, IRF1 (in the case of Cth), thereby contributing to the development of essential hypertension. Using a similar approach, they have identified several functional polymorphisms in the regulatory regions of Hmgcr gene in Spontaneously Hypertensive Rat (SHR, a rat model of genetic hypertension and related cardiovascular complications) as compared to its normotensive control, Wistar Kyoto rat (WKY). These studies provided new insights into the mechanisms of regulation of candidate genes in cardiovascular diseases.

**Systematic analysis of mechanisms of transcriptional and post-transcriptional regulation of susceptibility genes for cardiometabolic syndrome**

Dr. Mahapatra's research team has characterized the transcriptional and post-transcriptional regulation of several candidate genes for cardiometabolic syndrome (that is defined as a combination of risk factors, such as abdominal obesity, insulin resistance, dyslipidemia and elevated blood pressure). By using a combination of computational tools and cell culture experiments, they have identified the roles of transcription factors and microRNAs that are involved in modulating the gene expression basal and pathophysiological conditions including hypoxia and inflammation. For example, they have identified transcription factors involved in the regulation of heat shock protein Hsp70, renalase, monoamine oxidase A and B. Their discovery of the regulation of renalase gene by transcription factors Sp1, STAT3, and ZBP89 was the first report on the transcriptional regulation of renalase. Similarly, they, also for the first time, reported the involvement of miR-29 and miR-146 in the post-transcriptional regulation of mouse and human renalase gene expression. The role of miR-27a in the regulation of Hmgcr and miR-1224, miR-300 in the regulation of MAO-B gene expression at the post-transcriptional level are also their first reports on the regulation of Hmgcr and MAO-B genes by miRNAs. Interestingly, most of these genes are differentially expressed in human, rodent models of pathological conditions signifying their roles in cardiovascular complications. These findings are anticipated to develop novel therapeutic agents for clinical management of cardiovascular complications.

**In conclusion, Dr. Mahapatra studied several molecular pathways that are dysregulated in cardiovascular pathological conditions. His significant contributions in this area have implications for management of cardiometabolic disease states including hypertension, type 2 diabetes and dyslipidemia.**