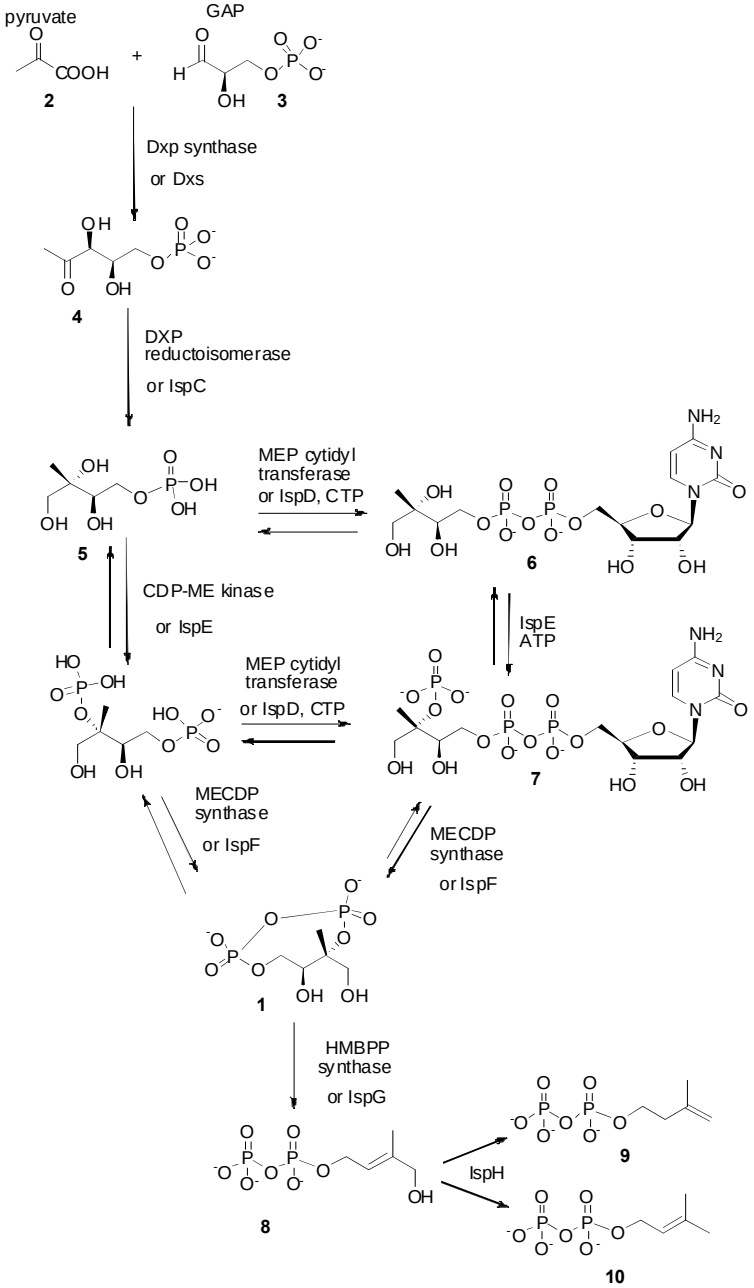
1. Antibiotic research-MEP pathway

Due to increase in drug resistant bacteria's, we are in need of new antibiotics through novel pathway. Methyl erythritol phosphate (MEP) pathway is an unique pathway for pathogens to synthesize essential isoprenoids and we targeted this essential pathway for antibiotic discovery. We have synthesized the chiral pure substrates (DXP (1-deoxy-**D**-xylulose-5-phosphate), MEP, CDPME (Cytidine di phosphate methyl erythritol), CDPME2P (Cytidine di phosphate methyl erythritol di phosphate), MEcPP (2-C-Methyl-D-erythritol 2, 4-cyclodiphosphate)) for the first time. All these compounds are not commercially available and we synthesized for the first time to optimize assays and determine inhibitors. We have also completed kinetic study of IspC, IspD, IspE, IspF protein with different pathogens for the first time. Finally we have discovered lead compounds to inhibit against *M. tb* IspD and IspE targets using this unique pathway.



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2. HIV Co-Infection research

There is no single drug for HIV-TB co-infection. In the process of drug discovery and drug development we discovered a new Gallium complex that reduces the growth of both HIV and TB. We have also studied the effect of novel drugs and nanoformulations effect against HIV-TB infected macrophages. In addition we found multi targeting mechanism of Ga in both HIV and TB. We have also synthesized new antiretroviral therapy nanoparticle. We have also isolated and characterized exosomes from HIV infected macrophages for the first time.

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b) I. Kadiu, P. Narayanasamy, P. Das, W. Zhang, H. Gendelman. (2012) Biochemical and biologic characterization of exosomes and microvesicles as facilitators of HIV-1 infection in macrophages. *J. Immunology*. 744-754. PMC Journal-In Process

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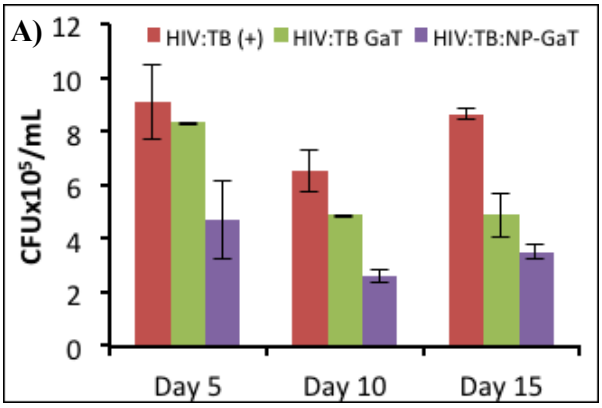

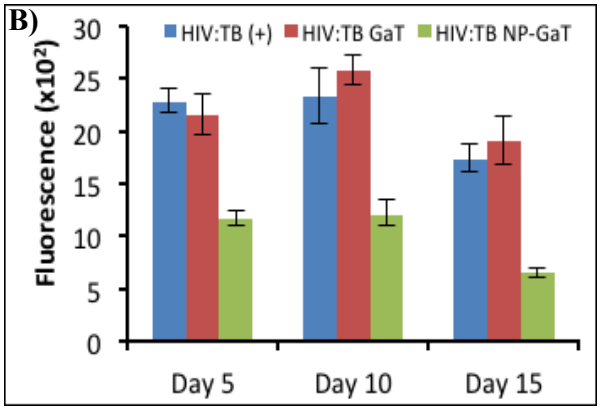

3. Antibiotic Research- Targeting Menaquinone biosynthesis and other Pathway

Since there is increase in antibiotic drug resistance, we decided to develop drug in non-traditional methods. In that regard we chose to inhibit menaquinone biosynthesis pathway and glyoxalase pathway. From our initial effort we have discovered a novel bicyclic lead compound for inhibiting the menaquinone biosynthesis. Similarly we have also discovered a new glutathione derivative for inhibiting the glyoxalse pathway for inducing bacterial suicide. Presently lead optimization for those lead compounds are undergoing in our lab.

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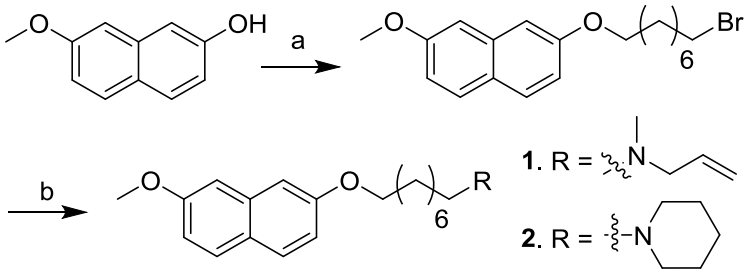
b) B. Edagwa, Y. Wang, P. Narayanasamy. (2013), Synthesis of azide derivative and discovery of glyoxalase pathway inhibitor against pathogenic bacteria, *Bioorganic & Medicinal Chemistry Letters,* 23(22), 6138-6140.

c) M. Kurosu, P. Narayanasamy, K. Biswas, R. Dhiman, and D. C. Crick. (2007). Discovery of 1, 4-dihydroxy-2-naphthoate prenyl transferase inhibitors: New drug leads for Multidrug-Resistant gram-positive pathogens. *Journal of Medicinal Chemistry,* 3973-3975.

d) M. Kurosu, S. Mahapatra, P. Narayanasamy, and D. C. Crick. (2007). Chemoenzymatic synthesis of Park's nucleotide: toward the development of high-throughput screening for MraY inhibitors. *Tetrahedron Letters*, 48, 799-803.

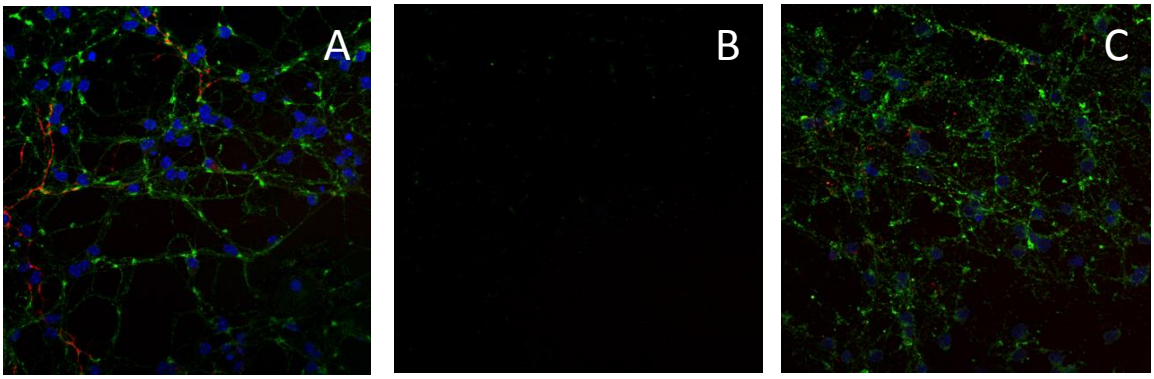


4. Neuroscience research

The glyoxalase system is a ubiquitous enzymatic pathway that catalyzes the glutathione (GSH)-dependent detoxification of methylglyoxal (MG) and other reactive dicarbonyl compounds, thereby playing a major role in the cellular defense against glycation and oxidative stress. It comprises two enzymes: Glo-1 and Glo-2. The accumulation of MG is highly deleterious, as this metabolite is one of the most potent glycating agents present in cells. It readily reacts with lipids and nucleic acids and with lysine and arginine residues of proteins to form advanced glycation end products (AGEs) such as the hydroimidazolone MG-H1, argpyrimidine, *N*-(1-carboxyethyl)lysine (CEL), and MG-derived lysine dimer. AGEs are implicated in various pathophysiological mechanisms, including those associated with diabetic complications (cataracts, retinopathy, nephropathy, angiopathy), aging, and neurodegenerative disorders. Also little is known about Glyoxalase pathway in brain. Our research is focused on drug discovery to upregulate the Glo1 and /or Glo2 in glyoxalsae pathway and detoxify the MG and improve the neuronal development.

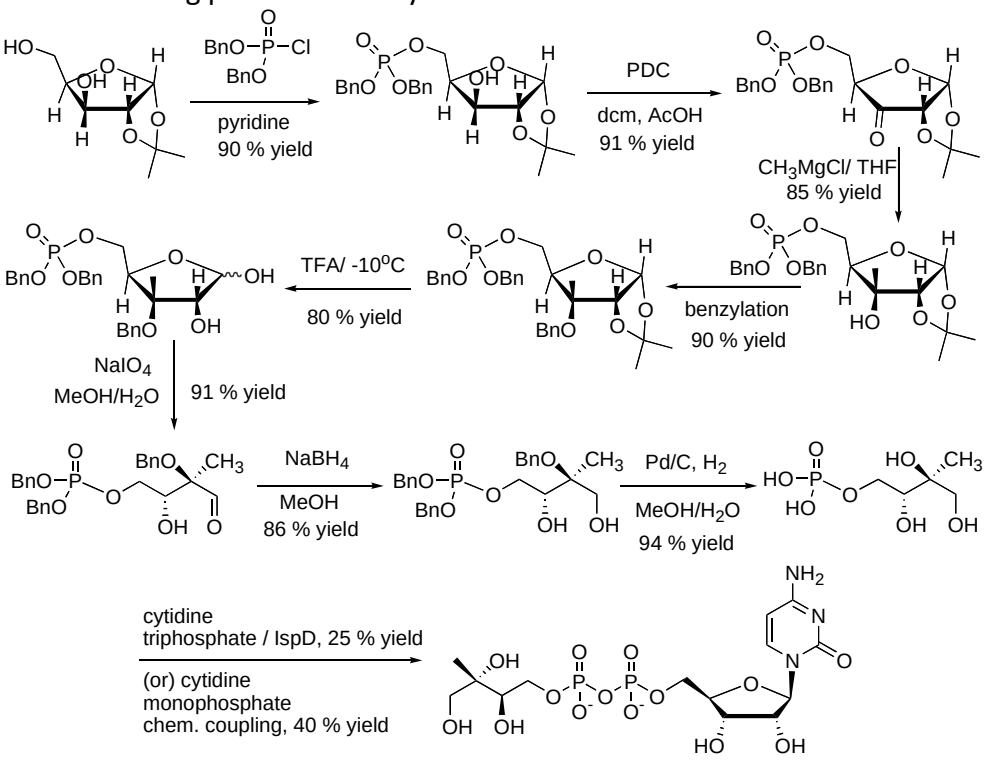
a) A. Epstein, P. Narayanasamy, P.K. Dash, R. High, S.P. Bathena, S. Gorantla, L.Y. Poluektova, Y. Alnouti, H.E. Gendelman, M.D. Boska. (2013) Combinatorial assessments of brain tissue metabolomics and histopathology in rodent models of human immunodeficiency virus infection. *J Neuroimmune Pharmacol.* 8(5), 1224-1238. PMCID: PMC3889226.

b) Bade, A.N., Zhou, B., McMillan, J., Narayanasamy, P., Veerubhotla, R., Gendelman, H.E., Boska, M.D., Liu, Y. (2015) Potential of N-acetylated-para-aminosalicylic Acid to Accelerate Manganese Enhancement Decline for Long-term MEMRI in Rodent Brain. *J Neurosci Methods.* pii: S0165-0270(15)00192-2. doi: 10.1016/j.jneumeth.2015.05.013



5. Metabolite, Drug and ligand study

For the first time we have synthesized chiral pure alpha, beta di-substituted amino acids. We have synthesized this novel compounds in gram scale and patented all of its derivatives. Earlier we have also published first asymmetric inverse electron demand Diels-Alder reaction, which is used for the synthesis of antimalarial and anticancer drugs. We have also established that chiral relay system will be more effective in inducing chirality for asymmetric reactions in conjugate addition. We have also established synthesis of selective allylic C-H oxidation using palladium catalyst.



a) M. S. Chen, P. Narayanasamy, N. Labenz, and M. C. White. (2005). Serial ligand catalysis: A highly selective allylic C-H oxidation. *Journal of American Chemical Society*, 127, 6970-6971.

b) M. P. Sibi and P. Narayanasamy. (2004). Chiral relay in enantioselective conjugate radical additions using pyrazolidine templates. How does metal geometry impact selectivity? *Synthetic Letters,* 13, 2421-2424.

c) M. P. Sibi, P. Narayanasamy, S. Ghorpade, and C. Jasperse. (2003). Enantioselective synthesis of α,β-disubstituted β-Amino acids. *Journal of American Chemical Society*, 125, 11796-11797.

d) G. Sundararajan, P. Narayanasamy, and B. Varghese. (2001). First asymmetric synthesis of quinoline derivatives by Inverse Electron Demand (IED) Diels-Alder reaction using chiral Ti (IV) complex. *Organic Letters,* 3, 1973-1976.