Integrated NMR and LC-MS based metabolomics approach for biomarker identification for radiation exposure

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Abstract

In the event of an intentional or accidental release of ionizing radiation in a densely populated area, timely assessment and triage of the general population for radiation exposure is critical. Despite decades of research, counter measures still lack. In this study, we describe the potential of integrated NMR and LC-MS approaches in evaluating the radiation biomarkers. Untargeted profiling by means of broad-spectrum, highly sensitive, UPLC-ESI-QTOFMS provides a comprehensive list of metabolites at one go in a single biofluid. Present study aims to discover new, as well as validate the previously identified metabolic signatures for whole-body irradiation in mice. The study comprised 33 C57BL6 male (8-10 weeks) mice distributed as 5Gy, 7.5Gy and controls having 11 each and irradiated through60Co gamma source. Urine samples collected post24 hrswere run in both ESI positive and negative mode. All the data were normalized by sum and were than pareto-scaled followed by multivariate analysis including PCA and PLS-DA. Of the total 1514 (positive) and 1764 (negative) peaks univariate analysis(t-test, $p<0.05$significant) revealed a total of 658 significant (positive) molecules with creatinine ($p=9.8\times10^{-5}$) and L-carnitine ($p=3.6\times10^{-8}$)from 5Gy whereas betaine ($p=2.0\times10^{-4}$), 8-hydroxyquinone ($p=9.6\times10^{-5}$) and L-carnitine ($p=3.4\times10^{-5}$) from 7.5 Gy. Out of 537 significant (negative) molecules taurine (4.7×10^{-4}) and Quinnolinic acid (6.3×10^{-4}) were from 5Gy. Present study thus validates our previously (NMR) reported significant metabolites citric acid, hippuric acid and taurine. The results thus lay foundation for high-throuput triaging by metabolomic biomarkers for effective medical management. Further pathway analysis also reveled results.

Biography:

Dr. Ruchi Baghel Ph. D (Biotechnology) my Ph. D research title was *"Pharmacogenomics of Antiepileptic drugs: Identification of predictive genetic markers for variable drug response in epilepsy patients".* Presently I am working as research associate in the Behavioral Neuroscience department of Institute of Nuclear medicine and Allied Sciences (INMAS), DRDO, Delhi. My work profile includes metabolic profiling of different bio fluids of mice and humans by using UP-LCMS QTOF SCIEX 5600. While the previous one year I have gained enough experience in various parameter optimizations, method optimizations of LC and MS for different types of biological samples. Presently I have worked on untargeted profiling of urine samples and soon we'll be working on targeted profiling (method development) of urine samples for few established metabolic markers of radiation.

Speaker Publications:

1. Vaishali Agrawal, **Ruchi Baghel**, Ajay K. Singh, Dharam Pal Pathak, Nidhi Sandal (2019). Development and validation of LC-MS method for the estimation of N-Acetyl- Tryptophan and its impurities under stress conditions. submitted to Chromatographia.

2. Rawat C, Guin D, Talwar P, Grover S, **Baghel R**, Kushwaha S, Sharma S, Agarwal R, Bala K, Srivastava AK, Kukreti R (2018). Predictors of treatment outcome in North Indian patients on antiepileptic drug therapy: A prospective observational study. Submitted to Neurology India. Neurol India. 2018 Jul-Aug;66(4):1052-1059. doi: 10.4103/0028-3886.237000.

3. **Ruchi Baghel**, Sandeep Grover, HarpreetKaur, Ajay Jajodia, ChitraRawat, ShamaParween, Kiran Bala, RachnaAgarwal, SumanKushwaha, Achal Kumar Srivastava, RitushreeKukreti (2016). Evaluating the role of genetic variants on response

to first-line antiepileptic drugs in North India: Significance of SCN1A and GABRA1 gene variants in phenytoin monotherapy and its serum drug levels. CNS NeurosciTher. 2016 Sep;22(9):740-57

4. **Ruchi Baghel**, Sandeep Grover, Kiran Bala, Harpreet Kaur, Ajay Jajodia, Shama parween, Chitra rawat, Ankit srivastava, Sangeeta Sharma, Suman Kushwaha, Rachna Agarwal, Achal Kumar Srivastava, Ritushree Kukreti (2016). Synergistic association of presynaptic neuronal genes with cryptogenic epilepsy in North Indian population. Brain Behav. 2016 Jun.

5. **Ruchi Baghel**, Ajay Jajodia, Sandeep Grover, RitushreeKukreti (2014). Highlights from latest articles directing the need of focus towards a new gene set for better drug response prediction of epilepsy patients. Pharmacogenomics. 2014 Apr;15(5):581-6. doi: 10.2217/pgs.14.11.

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