CHAPTER: 05

TISSUE METABOLOMICS

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Ch.Id:-ASU/GRF/EB/IASINAM/2022/Ch-05
DOI: https://doi.org/10.52458/9789391842741.2022.eb.grf.asu.ch-05

Tissues: The tissue biopsies have always been widely studied for the identification of pathology associated with it especially in case of cancer or chronic inflammations. The quantum of information a tissue biopsy carries in itself has been immense and therefore, it is an extensively explored biological sample at genetic, proteomic and nowadays at metabolic level. In metabonomics, the tissues are either subjected to extraction procedures or are analysed directly by HRMAS NMR spectroscopy. MAS has an added advantage of maintaining tissue integrity for other genomic and mRNA studies from the same tissue biopsies. Moreover, minimal sample preparation has led to numerous biomedical applications for investigation of breast cancer affected tissue biopsies (Sitter, Sonnewald et al. 2002), brain tumors (Cheng, Chang et al. 1998; Warren 2004), liver transplants (Duarte, Stanley et al. 2005), prostate cancer (Taylor, Wu et al. 2003; Santos, Kurhanewicz et al. 2010; Dittrich, Kurth et al. 2012), rat intestine development (Wang, Tang et al. 2005) and many more studies including toxicological effects on tissues and its biochemical characterisation (Wang, Bollard et al. 2006). Such studies are endowed with an insight about disease biochemistry and provide a better understanding of altered metabolic pathway which could be exploited for targeted drug delivery. However, care must be taken while analyzing tissue biopsies to avoid the pre-analytical bias from the data acquired such as in case of tissues with heterogenous composition multiple sampling must be done for proper assessment of disease and it also ensures reproducibility (Cheng, Anthony et al. 2000). The factors which might affect the integrity of tissues come up significantly with the various pre-acquisition stages like improper storage, freeze thaw cycles and during acquisition.

Storage: Tissues are rich source of enzymes due to the presence of different metabolic compartments. These enzymes cause perturbations in biochemical composition of tissues even after their resection, therefore, minimization of enzymatic processes after tissue resection is of paramount importance for removing any pre-analytical bias. The optimum temperature for enzymatic activity ranges from 40-45^{o}C and therefore the storage should be at lower temperatures. The room temperature storage should be avoided as the enzymatic reactions keep occurring with slower rate of reaction. The best way of storing a resected tissue is snap-freezing under liquid nitrogen environment as it solves both the purposes of minimizing enzymatic activity and biochemical degradation (Beckonert, Coen et al. 2010; Srivastava, Roy et al. 2011). The long term effect of storage at -80^{o}C on prostate cancer tissue biopsies were studied for 32 months and it was found that frozen storage induced metabolite perturbations were insignificant statistically and are less critical than the influence of pathological heterogeneities present in a tissue (Jordan, He et al. 2007).

The storage of prostate tissue biopsies in glycine buffer solution was evaluated by Bourne et al. for estimation of leakage of metabolites of tissue in buffer solution after its storage and freeze thaw cycle. The biopsy was suggested to be removed from buffer while MR measurements as the leakage of metabolites result in 55 to 98% loss of metabolites of tissues in buffer solution (Bourne, Dzendrowskyj et al. 2003). Therefore, the biopsies should be snap-frozen in its native state in an eppendorf tube with no buffer solution. This will assure only the morphological changes in cellular structures of tissue and no leakage of metabolites from the subject of interest.