NMR-BASED METABOLOMIC ANALYSIS OF BLOOD PLASMA AS A PANCREATIC CANCER DIAGNOSTIC TOOL

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Pancreatic cancer (PC) is well known for high mortality, the 5-year survival reaches only 5 %. This is mainly caused by asymptotic course or unspecific symptoms. The poor prognosis can be improved by early diagnosis. In this context, the relationship of PC to diabetes mellitus should be investigated as diabetes or impaired glucose tolerance had been observed in 80 % of PC patients. This specific type of diabetes mellitus is characterized with increased risk of PC development and it is called pancreatogenic diabetes (T3cDM). Since its development is similar to the most prevalent type 2 diabetes mellitus (T2DM), T3cDM is often misdiagnosed. T3cDM patients are associated with an up to 7-fold increased risk of PC development. [1] The differentiation of T3cDM-T2DM among recent-onset diabetes mellitus (RODM) patients may play crucial role for the early PC diagnosis and thus improving the prognosis of this fatal disease. NMR metabolomics may facilitate the solution of this complicated problem of recent clinical diagnosis. [2,3]

In this work, ^{1}H NMR metabolomic analysis of blood plasma was used as an alternative approach for early PC diagnosis in RODM patients. Based on concentration profile of 58 metabolites, a discrimination of PC patients from long-term T2DM patients was achieved. A specific biomarker panel of eight metabolites was proposed and successfully tested for PC diagnosis against T2DM patients and healthy controls. Moreover, a prediction model for the identification of risk individuals for PC development in RODM group was developed and the patients likely suffering from pancreatogenic diabetes were identified. Six of 59 RODM patients had similar metabolic characteristics as PC patients and their health conditions were therefore re-examined. The found pathological changes correlated reasonably with our findings. Recent results also indicated subtle metabolic changes among individual PC clinical stages that could be used for their differentiation in future.

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REFERENCES

[1] Pannala R., Basu A., Petersen G. M., Chari S. T., *Lancet Oncol.* **2009**, *10*, 88–95.

[2] Michálková L., Horník Š., Sýkora J., Habartová L., Setnička V., *Analyst* **2018**, *143*, 5974–5978.

[3] Michálková L., Horník Š., Sýkora J., Habartová L., Setnička V., Bunganič B., *J. Proteome Res.* **2021**, *20*, 1744–1753.