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To whom it may concern

RE: REPORT ON ERNDIM TRAINING GRANT AWARDED TO MS S. BARTLETT.

First and foremost, I would like to express my gratitude towards ERNDIM for granting the financial support to receive training in the Netherlands. I would like to thank the remarkable Dr George Ruijter for hosting me and facilitating my training at the Department of Clinical Genetics at Erasmus Medical Center in Rotterdam.

The primary purpose of the visit was to receive training with regards to the UPLC-MS/MS method for the quantification of glycosaminoglycans (GAGs), for the diagnosis of mucopolysaccharidosis (MPS). This method is intended for implementation in our metabolic laboratory (PLIEM) in South Africa (www.pliem.co.za). The laboratory forms part of the Center for Human Metabolomics at the North-West University, South Africa, which is dedicated to meeting the demands of the Health Sector through innovative and sound analytical service and strives to find new advanced methods to benefit all.

Driven by this spirit, the laboratory sought to improve the method by which MPS disorders are currently detected.

Background and reason for visit:

Mucopolysaccharidosis (MPS) describes a group of lysosomal storage disorders that could have devastating effects on those born with these type of inherited enzyme-deficiencies. Diagnostics involve screening for the associated metabolites, excreted in the urine (GAGs) and followed up with specific enzyme testing. Any deficiency of the involved enzymes will block GAG degradation, resulting in the accumulation of GAG macromolecules in the cells, which contain specific sulfated carbohydrate residues that can cause alarming dysfunction. Screening for GAGs at PLIEM laboratory includes a dimethylene-blue (DMB) spectrometric assay and a one-dimensional gel-electrophoresis. The DMB-assay is not sufficient for diagnosis and the electrophoresis method has many pitfalls and shortcomings, resulting in false positives and negatives and also has a prolonged reporting time.

The advantages of utilizing liquid chromatography, coupled with tandem mass spectrometry (LC-MS/MS) for this purpose, has been explored extensively in literature and concluded to be a sensitive, simultaneous and effective technique, which will aid in correct diagnosis of MPS patients (Chuang *et al*.,2014).

The need for an improved method was clear to us and implementing the UPLC-MS/MS method has been in the pipeline for quite some time now. It is only with the help of ERNDIM and the kind staff at Erasmus MC, that we now are able to implement this improved diagnostic tool.

Training@Erasmus,MC:

I received excellent assistance in the analytical and statistical aspects of the method and thorough explanations regarding the set-up on the instruments. Dr Ruijter spent time with me on the interpretation of results and gave valuable insight into the different types of MPS disorders and how to identify a truly abnormal result and differentiating between normal and affected individuals.

In addition I was fortunate enough to observe the DMB robot-assay, the thin layer-chromatography (TLC) for oligosaccharides and the method for sialic acid analysis.

A special thanks to Ms Linda van Dorst, who was tasked with training me in sample preparation and quality control. Her dedicated spirit and knowledge in the field made a tremendous contribution to my visit. Also, a special thanks to Mr Jeroen van den Bosch who assisted me in understanding the background and features of the instruments. I also would like to extend my gratitude to the rest of the staff, who made my stay pleasant and unforgettable.

Conclusion:

The training was thorough, enriching and left me with the required knowledge to successfully and confidently apply this method. I am glad to report that implementation of the new method is already in progress and will form part of our diagnostic arsenal in the very near future.

This opportunity that ERNDIM has made possible, has greatly benefited myself and the scientific community in South Africa. We hereby express overwhelming gratitude to ERNDIM for the generous contribution.

Regards,

Sonja Bartlett

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