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Dr. Yavuz OKTAY
Co-PI

12th June 2018

Dear Professor Hanna

International Centre for Genomic Medicine in Neuromuscular Diseases Turkey

We confirm our participation in this new MRC strategic initiative if awarded according to the following principles with which we jointly agree:

Benefits for research and for the health of NMD patients

We confirm that an International Centre for Genomic Medicine in Neuromuscular Diseases would have very significant and long lasting research and health benefits for our patients with NMD.

Defining our patient cohorts by genotype will allow us to:

- Increase the number of patients with a precise genetic diagnosis the results of which will be conveyed to patients, according to the local arrangements, through clinical services we lead
- Discover new genes
- Provide more accurate advice and counselling to patients and families
- Implement international care guidelines for screening/managing patients on a rational basis
- Make the case locally more strongly for access to appropriate screening and simple health interventions including cardiorespiratory, gastroenterological, metabolic and physiotherapy.
- Identify patients who will benefit from using repurposed cheap drugs for some conditions such as channelopathies and congenital myasthenias based on a precise genetic diagnosis
- Have "trial ready" cohorts optimising our interactions with pharma and industry and visibly expanding the global market for use of new therapies now developed and which will be developed in the next 5-10 years

Long lasting benefits of training and bioinformatics platform:

- **Training a new generation of clinical academics** with strong UK support networks who will become the leaders of genomic medicine and specialist care delivery in and who will develop national networks of excellence and be a transformational output from this initiative
- **Sharing genetic data:** the openly shared bioinformatics data platform will be a major advantage this consortium and will empower all clinicians and clinical researchers to analyse their own patients' NGS data on the RD-Connect genome phenome analysis platform and derive molecular diagnoses. They will continue to do so beyond the funding period of the centre. Moreover, they will be able to educate and train other healthcare professionals in their countries to make use of NGS data and bioinformatic platforms for the benefit of their patients.

These developments will only happen through this new initiative and will add major value to our existing developing neuromuscular services enabling us to become a centre of excellence which will spread good practice nationally and enable sustainability after 5 years.

Building Cohorts

We assess over 5000 patients per year with NM diseases and with the support of clinical fellows we commit to recruiting, phenotyping and genotyping at least 4000 patients into the cohort over the next 5 years. We understand that recruiting to the cohort is an essential deliverable for our centre and that it will be reviewed monthly. We already have cohorts of muscular dystrophies, spinal muscular atrophy, hereditary neuropathies, hereditary spastic paraplegias, and mitochondrial disorders.

Appointing fellows

There will be major competition for such prestigious fellowships. We undertake to advertise and appoint such fellows in conjunction with the training and fellowship committee chaired by Professor

Reilly during the 6 month period prior to the grant initiation. We understand that appointing fellows is an essential deliverable of the programme. We will ensure fellows have two local mentors (a clinical mentor and a science mentor). We will minimise the risk of fellows moving abroad after training by ensuring they are offered a position at the end of the fellowship to secure a permanent legacy of specialist clinical academics in neuromuscular genomic medicine for patients. Furthermore we note that during the two 6 month training periods in the UK they will not have full GMC registration but will only have observer status.

Adopting standardised clinical work ups

We have extensive experience in evaluating patients with neuromuscular diseases at our Centre. We have expertise in recognised diagnostic criteria for NMD including ENMC diagnostic criteria. We will train the fellows in detailed neuromuscular patient evaluation and they will be trained in the Phenotips HPO by the UK partner team during their brief period in London.

Delivering healthcare solutions

We confirm our centre is recognised as providing more specialised care for NMD patients in our country although we aim to be a centre of excellence by international standards. We confirm increasing the number of patient with a precise genetic diagnosis will be a significant healthcare benefit in our centre and we will be in a position to implement simple standards of care that are required following a precise genetic diagnosis. Furthermore it will allow us to build genotyped trial "ready cohorts" which we can follow up. For precisely defined genotyped cohorts where new treatments become available as is likely over the next 5-10 years we will be in a strong position to pursue governmental bodies and healthcare funders to enter into partnerships e.g. with pharma to make drugs available to our NMD patients.

Data sharing and ethics approvals

All data will be pseudoanonymized. We are fully committed to data sharing through the proposed platform. We recognise that data sharing is important to the project and will be made possible following an agreed embargo period and under controlled access conditions. We recognise that all data will adopt the General Data Protection Regulations of the EC 2018. We confirm we will secure all required local ethical approvals before MRC funding commencement.

Sustainability following the end of the grant award

The initial investment from the MRC in this initiative will be a major catalyst for our centre to secure additional outside investment and ensure sustainability. By being part of this application we have already been able to secure onward support for the fellows at the end of the grant to ensure they are a lasting legacy of neuromuscular expertise.

Our participation in this programme will enable us to leverage institutional and national funding schemes. We confirm we agree to all the above principles

Yours sincerely

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Turkish Lead PI and on behalf of all Turkish investigators

Turkish Co-PI Dr. Yavuz ÖKAY

Professor Michael Hanna On behalf of UK PI's