## Present

In person: Nessa Carey (NC) [Independent Chair], Helen McShane (HM) [Co-Chair], Oliver Harrison (OH), Mike Whelan (MiW), Jan Wolber (JW), Laura Ferguson (LF), Antony Galione (AG), Paul Cox (PC), Giles Sanders (GS), Liisa Chisty (LC), Matthew Carpenter (MaC), Katharina Ramshorn (KR), Toni Day (TD)

Online**:** Matthew Wood (MaW)

## Officers

Translational Research Office (TRO) (in person): Deepak Kumar (DK), Kavita Subramaniam (KS), Fiona Story (FS), Vlada Yarosh (VY), Oliver Rughani-Hindmarch (ORH), Deborah Thomas (DT)

## Apologies

Eleanor Stride (ES), Fadi Issa (FI), Paresh Vyas (PV), David Clifton (DC), Heather Roxborough (HR)

* Welcome and Introductions to Committee Members & Translational Research Office
* Minutes of previous meeting.
* Budget for 2024-2025.
* Conflict of Interest Declarations.
* Ranked list of proposals.
* AOB
* Feedback on MLSTF planning and transformational changes for this year
* Update on the UKRI IAA status
* Planning for the next round of MLSTF
* Diagnostics expertise to be added on the MLSTF committee

Please note, these AOB points will be followed up/addressed via email giving an opportunity for the committee to voice opinions and give feedback. The TRO will then collate, process and communicate outcome back to the committee after discussions with Chair and Co-chair.

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| --- | --- | --- | --- |
| TRO Reference Number | Application Number | Applicant | Feedback |
| 39 | 14946 | Elena Stylianou | The panel felt that this proposal was outstanding and superbly written. The proposal has pre-existing data, a clear plan forward with a clear rationale for the work packages proposed within the MLSTF proposal that would lead to a value of inflection point towards Ph1 clinical trials. The team is outstanding, and the IP strategy and potential is clear. |
| 28 | 14971 | Jagdeep Nanchahal | The panel felt the project was very clearly in remit, and well worth funding with a good IP position. They felt the focus on mitochondrial dysfunction was an area of high current interest.  The panel suggested that an early career researcher could be brought in on the project, to potentially be mentored by the lead PI’s to help develop the progression of early career researchers in translational research. |
| 9 | 15008 | Sally Collins | The panel felt that overall this was a strong proposal with huge translational, clinical and commercial impact. The proposal was well-written with a strong IP position and an excellent downstream path and plan towards commercialisation. The panel was in agreement with all comments provided by each reviewer. |
| 45 | 15010 | Ellie Tzima | The panel felt this was a well-written and strong proposal with potential to create huge clinical impact. The background data is compelling, and the data generated within this MLSTF proposal would lead to strengthening the IP strategy and applications towards external translational funding schemes. The panel felt that the proposal outlines an excellent use of funds.  The panel did feel that the applicant could consider contracting out some of the work rather than doing it all in-house. |
| 47 | 14941 | Paresh Vyas | The panel were happy with the project and felt it was a strong proposal with the potential to reach high impact. All agreed it should be funded. |
| 7 | 14765 | William Clarke | This is a very interesting proposal using brain imaging software to help with the diagnosis. Good collaboration with Manchester. The application is well written and builds on existing IP. The project will be impactful.  The panel has concerns that the FSLT is providing data for more and more indications, but they are not progressing with the commercialisation of the technology.  There might be a bottleneck here. They have trademark but no underlying patents (it’s software therefore copyright). There is a lot of competition and so they need a really professional application for their technology, they have more and more uses but no solid way of implementing it. There may be some issues with the software and so there may be a high residual technical risk, we have to see risk going down. They’ve had a few project surgery sessions and the experts suggest to put this in place but nothing has happened.  Another risk about the software not being able to detect the difference between ‘normals and not normals’ needs to be addressed and not left until the end.    **The panel strongly recommends the applicant contacts the TRO as soon as possible to set up a meeting with OUI and the experts (Jan Wolber, Toni Day and Oliver Harrison).** |
| 21 | 0014950 | Thomas Lanyon-Hogg | The panel very much liked the application. They understand there is an issue with antimicrobial resistance and the need for new antibiotics. They believe this project is innovative and allows existing antibiotics to become effective again.  The panel did however question whether the modification will affect efficiency, and whether this needs to be considered for future scale-up.  They also felt that the regulatory challenges may not be as straight forward as described in the application. As although the molecule is based around an already existing molecule, it will not be treated as such from a regulatory standpoint. There will be regulatory processes for this project and this will lead to higher costs. They feel the applicant may benefit from input from a regulatory expert, to improve their regulatory understanding. The applicant may wish to consider contacting the Experts in Residence network run by the TRO |
| 48 | 14743 | Richard Williams | Panel highlighted that this is a very hot topic and an exciting field. Engineered anti-inflammatory where the area of inflammation is seeing a lot of innovation and panel liked the TNF angle. Panel were encouraged that the team have some preliminary data already available and think there could be broad application for other diseases. Panel would like the applicant to think of accelerating this work (through MLSTF or other) to get first in human much sooner as there can be a lot of competition on the market by the time they get to clinical stage. Panel suggested perhaps to think clinical impact should be into earlier care pathway.  Panel also highlighted there needs to be more information on mechanism of action, if this has not been done already. Should applicant need assistance on this aspect in the future, this can be facilitated by the TRO through a 1:1 with one of their Expert in Residence who is aware of this proposal.  Panel members from OUI have voiced concerns that they do not have any information on the applicant’s background IP therefore urges the team to engage with OUI **as soon as possible** to discuss aspects of protection considering the competition in this space.  Panel as a whole agrees to fund this application with the condition of funding being the research team has to consult with OUI in the first instance with a TRO representative present. |
| 30 | 14933 | Graham Ogg | The panel were overall very happy with the proposal. However, they did state that there could have been a bit more preliminary data and a clearer commercial pathway in the application |
| 8 | 14744 | Lei Clifton | This is a very interesting proposal and technology that would  that would give a lot of time to visit GPs. What is also promising about this proposal is that the team have an existing partner.  The commercialisation route might need to be thought through a bit more as the team haven’t identified what the end result is with regards to commercialisation of this technology. The panel is in agreement that the application would have benefited from having more usability interview elements built into the proposal. Need to better understand: What are pain points that the clinicals face? Do we really understand them? Are we developing a solution that addresses those? The team need to be certain that the GPs will definitely be able to use it and that there is a clear route to market, to avoid creating a good solution that nobody wanted in the first place.  There is also a regulatory pathway that needs to be considered and understood because if you are putting in a clinical decision support, then it needs to go through the appropriate regulatory calls. Might be worth getting decent feedback from the regulatory body.  **The panel requests that the team contact the TRO as soon as possible to arrange a meeting with the expert, Dr Oliver Harrison, who will help the group address the concerns raised by the panel on user experience, regulatory and commercial pathways.** |
| 13 | 0015017 | Jennifer Frommer | The application would have benefited from being written more like a translational than a research proposal with more clarity on how MLSTF is the right way to address the research problem.  The team should have a bit more clarity on whether they are developing an ASO or treatment for SMA. |
| 26 | 14957 | Karl Morten | Despite reading like discovery research and having quite critical reviews from reviewers, the team is good. Risk is present and acknowledged but given the large unmet need this will be a high reward. Panel members agreed they liked the approach and proposal on the science part but agrees that they don’t posses enough understanding on the IP position.  Comment from OUI as follows: OUI have tried to spin this work out before but didn’t work as it was still at an earlier stage, and it can be tricky. Seeing its in oncology arena, and early stages, there is still 14 years left on the patent that is currently supported by WRH.  Panel also agrees that these currently proposed work packages might potentially fill the gap as applicant have returned after 4 years. However, panel doesn’t have enough understanding if substantial progress has been made to make it’s a more commercially interesting proposal.  Following further due diligence by the TRO, panel is pleased to fund this work after confirmation that the application submitted in 2021 is different from the one currently submitted, is focussed and at an inflection point. |
| 22 | 0015015 | Valentine Macaulay | The strategy of the project is to antagonise the effects of insulin-like growth factors, not by blocking receptors, but by generating cyclic peptide. The rationale behind this is that IGF promotes cell growth in a number of tumours, prostate cancer and frailty. This is a better strategy than blocking the IGF receptors, as it will less likely have effects on glucose.  This approach has failed in the past, but it has great potential in the future. Industry has become lukewarm on this target as previous clinical trials on the target have failed. Colleagues from Astra Zeneca Oncology were not positive as this feels like a very long way from being a drug for a target that people are sceptical about.  An interesting target and their strategy has advantages over competition. But they are still at the stage where they are trying to generate the right peptide, which seems to be a bit too early. The project could be judged better after the peptide is generated and they have taken it into in-vivo studies. The team talk about the pill, but there is no information about the pharmacokinetics. The project presents with a great strategy, but they should show a few more studies before coming into this. Currently, the project is not proposing studies in animals, hence lack of pharmacokinetics data.  The team have identified a lead, but it is not clear is they have any back-up series. More information is needed on why this would be a good target for a drug.  This project is of interest, but the team haven’t really either convinced on the background story or convinced in terms of if they are really doing the right things that need to be done. The project at this stage is missing some key components that would give us confidence. |
| 33 | 14948 | Carlo Perrone | The panel liked the proposal submitted by the ETI applicant. There is a clear LMIC unmet need with a clear solution proposed. The panel do feel that the applicant must seek support from the TRO and leverage expertise advice from the Experts. |
| 32 | 0014942 | Sarah Pendlebury | The Panel felt that although the project was interesting and may have good clinical impact, the chances of commercialisation were limited as there was no clear use case. They also had some concerns with the regulatory aspects of the project and were unclear on the long-term direction of the work.  The panel also felt that the project may be out of remit, as the proposed outline was not translational enough in nature. They suggested that the project may be better suited to BBSRC or EPSRC grants. The panel has also suggested that the applicants to get in touch with the TRO who can facilitate a meeting with Dr Jan Wolber (an Expert in Residence) to provide detailed feedback on the tissue issues based around the application. |
| 37 | 0014976 | Annette Schuh | The panel felt that this was an interesting proposal for a clear unmet need. However, the proposal is out of remit and is at a very early-stage. The panel questioned whether the mouse data would be sufficient to take the project to the next value of inflection point. Currently there are too many risks associated with the project. The panel also questioned the novelty of the approach to translation as similar approaches are commonly being pursued. |
| 5 | 0014890 | Arjun Chadna | The panel liked the project for its use in LMICS and acknowledge the project as being part of a good consortium with strong expertise. They also thought the project had a good chance of identifying a target. However, they questioned whether the test could be used as a diagnostic, and thought there was a low probability of success as a diagnostic tool, as there may be issues around validation. They also felt that it would be difficult to patent and there would be no incentive to patent as the main use is in LMIC. The panel also stated that the project may be too early stage, and is missing the key translational aspect. |
| 36 | 14998 | Angela Russell | Panel agrees this is an excellent proposal; There are a lot of competition in exon skipping and its failing. End points are difficult due to patients’ deterioration therefore it is a big ambition. Indication for DMD is not licensed in Europe.  However, panel’s main concern is about the broad scope of the work from the team’s already existing DPFS funding in place for a very similar work, therefore unclear on what makes this MLSTF different. If the applicant can show and assure that this project is completely different from the DPFS project, the panel will be happy to fund in principle.  **Follow up since MLSTF panel meeting**: Following TRO’s further due diligence, the applicant has confirmed that the work packages proposed is different than that from the DPFS work. Panel agrees to fund this work in its entirety. |
| 23 | 0014628 | Robert MacLaren | The proposal is presented by a well-known and excellent group developing retinal gene therapies. The panel is very positive about this application and agreed that the rationale of this proposal is sound. The proposal aims to test how mini circle technology for the delivery of large DNA genes where these cannot be packaged within a small AAV vector. The approach the team is proposing to test is using electroporation, so there might be issues around translatability of this, though unlikely considering the context of the application and what the team are aiming to do. The proposal aims to test this in the context of one of the genes related to retinitis pigmentosa which cannot be delivered using standard AAV.  The panel agreed that the experimental detail provided should be more in-depth. It is critical to show what exactly the milestones and endpoints to demonstrate whether the electroporation is successful in terms of the gene therapy and translation into protein. These milestones that would constitute success are missing.  The panel are very keen support this application on the condition that the applicant provides a more detailed description of the work packages (Note: has been successfully actioned). |
| 35 | 0014913 | Thomas Roberts | The panel had strong reservations in investing funds for a screen to validate more candidates although 4 candidates are already identified by the applicant. The panel also felt that overall, the proposal is too early. |
| 42 | 14647 | Huiling Tan | Even though it is high risk, the proposal was very clear and in remit. The team are also fairly advanced with their understanding of the regulatory processes involved.  This is an important research project which can potentially save neurologists a lot of time to achieve a clinically meaningful outcome. The application is good, even if the IP position isn’t very strong.    The OUI currently have 13 patents on DBS, for which they cannot find commercial partners and there are a lot of very similar projects. The project has a great potential, but the team needs to have the technology tested on humans to prove it useful, which will be difficult to do. The project is strong but has a low commercial potential.  However, if there is a low number of patients, which might hopefully increase as the DBS becomes more common and implementable, and even if Oxford doesn’t commercialise this, there are no IP issues which will stop the project from going forward.  There will be clinical and patient impact but not in a commercial setting, and the panel is still keen to support this. |
| 31 | 0014972 | Bartlomiej Papiez | Hyperpolarised Xenon MRI is an increasingly common intervention aimed at very common conditions. Using this technology in an MRI scanner for making it simpler, cheaper and easier, so this is a good translational proposal with a good use case and a pathway for future commercialisation.  This technology is already approved for ventilation imaging as a drug device combination in the US. The proposal is translational, but it is a drop in the ocean of what you need in order to establish this. It is not clear what the product from Oxford would actually be, because there is already a company in the US which is already working with this technology. IP landscape is difficult, it may be very difficult to patent. |
| 18 | 0014926 | Jasmina Kapetanovic | The panel agreed that this is an interesting proposal though there are some complex issues around the CRISPR IP. The project is quite early, so it would be a long time before it actually comes into commercial fruition, so that is the main issue. Too broadly written, too early, though very innovative. There is limited preliminary data or information about the safety concerns. But as an approach and a method, the panel thought it was very innovative. There is even a sentence about the downstream components of the phototransduction which signals that the team don’t actually know if there is a single gene editing approach. So, the team might need to edit the entire pathway. And the idea of activating multiple genes in a pathway in humans would have so many safety concerns. This would be more of an experimental proposal rather than a translational one. |
| 25 | 0014977 | Adam Mead | The Panel felt that although the project had a good approach, the application was lacking in quantitative expected outcomes and lacked further experimental detail.  The Panel also had questions regarding the commercial viability of the project and thought that the research might be better suited to a licence instead of a spinout. They also questioned whether CRUK could fund this type of proof-of-concept research. |
| 43 | 15019 | Walter Taylor | The panel felt that the proposal was well-written with potential to reach high-impact. The work packages proposed are appropriate and is critical to the downstream development of the end product.  One concern that the panel highlighted was the change in the preferred formulation route by the WHO. This may result in the applicant’s formulation being excluded from the WHO’s recommendations. The formulation does need to be pre-qualified by the WHO. A pathway to formulation will need to be shown. |
| 2 | 0014963 | Martin Bachmann | The greatest concern of the panel was Oxford’s freedom to operate and use the technology commercially. Further clarification was needed for the relationship with Bern/Swiss National Science foundation. Downstream business plan is unclear. |
| 24 | 0014953 | Philip McGuire | This is a pilot study that has no data at this point. The panel is also not convinced by the applicant on their commercialisation plans. |
| 40 | 14981 | Pawel Swietach | The panel agreed that the proposal has a great unmet clinical need that is being tackled with a strong translational potential to create impact. The commercial partnership is valuable and pivotal in achieving the desired value of inflection point. The panel agree that the proposed work packages are the next key killer experiments which allow derisking before moving to the next stages of development for which they have a manufacturer already lined up (Abingdon Health). |
| 29 | 0014894 | Darragh O’Brien | The panel understands from communication with AZ that the neuro team have an interest in this approach and area. This is an impressive application for a major unmet need and AZ has been trying for years. It’s a hot target. If the group could get this project to work, would be fantastic, also supportive that the applicant is an ETI.  Panel agrees that while the science is great, there is a need to work with external partners or research council, and to address the concerns from reviewers above. Panel also agrees that the proposed work is still at an early stage and has to be appropriately de-risked before MLSTF.  Panel also HIGHLY recommends the applicant to reach out to OUI to talk about the IP and protection of the lead compound series, as this is a hot topic and applicant should seek out advice on the IP strategy.  Panel member from AstraZeneca (AZ) has requested the following feedback from AZ’s Neuro team to be shared with the applicant:   1. *The approach- is it interesting in the field?*   *Absolutely – very interesting and smart approach they have taken.*   1. *Would it be wise to fund this work based on what you know of the field?*   *Given cost and what they have achieved so far and plan to do next, yes.*   1. *Are AZ neuro interested in following up for a potential partnering discussion?*   *In principle, yes, but as always it does depend on overall outcome of planned studies, along with existing data generated so far etc.., but the experimental plan and drug discovery cascade is very innovative and interesting, and in general this target space is in AZ neuro’s overall strategy but that also needs to defer to AZ’s overarching strategy for neuroscience in an external partnering space, but in principle yes we are highly interested and already invested in this biological area for AD  (not this target I must stress)*    *If the applicant and the team feel appropriate, AZ’s neuro team would like to continue discussions and have a project update to follow this project. There is also willingness to provide some kind of mentoring/advise from AZ neuro colleagues if this would be of help.*  Note: The Chair and co-chair of MLSTF Panel are pleased with the interest shown by AZ for this applicant’s proposal. The advice is to have TRO put the team in contact with BPO and Research Services for appropriate CDA/NDA in place if the team would like to / happy to follow up discussions with AZ. For the research team’s knowledge, AZ currently already has a pre-existing CDA in place with the TRO for discussions with researchers via the Experts in Residence network therefore these conversations can be expediated. |
| 27 | 0014989 | Manisha Nair | Panel agrees there is a good translational pathway however it is not fundable in its current format. It isn’t right that the team is proposing  doing market research after prototyping is done. |

## AOB:

The panel suggested the following improvements:

* Application pack to be bookmarked for efficient searching of assigned applications to revie.
* The briefing meeting held for the reviewers was good and incredibly useful. This will be held again for the next round of MLSTF
* The ETI route has been a great success and the pilot has demonstrated a clear unmet need. Moving forward, the panel have strongly recommended a mandate for all ETI’s to connect with the TRO at grant application stage
* The scoresheet and scoring system was great and the panel are happy to move forward with this for future rounds of MLSTF.
* The panel have suggested to remove the confidential abstract as this is a duplication of the non-confidential abstract.
* Some members of the panel expressed strong views on the potential of a pre-funding triage process to be implemented.

Planning for the next round of MLSTF:

* DK: We have another call later in the year. As the volume of funds is increasing we are requesting the MLSTF committee meets twice a year.
* We need to consider asking applicants to declare if the project is submitted elsewhere (on both forms - MLSTF and John Fell Application funds) and perhaps whether we should not allow parallel submissions. ***Applications, scores and reviewer comments may be shared with other internal University panels to ensure maximum value for money.* [to be added to the call text]**
* Proposals discussed for funding decision after the panel meeting - as there were excess funds, that were going to be discussed:
  + Jennifer Frommer – Funded, ETI.
  + Karl Morten – Application submitted in 2021 different from the currently submitted, focused and at an inflection point.

Due diligence requested:

* + Robert Maclaren (RM) - No milestones or endpoints highlighted in the application. Can’t be funded as it stands, as more details are required on the milestones of this project. The panel would like toget RM to provide more detailed work packages (Gene expression – confirm). The TRO will ask RM to provide more detailed work packages then the project would be fundable.

The panel have confirmed this funding is conditional, if further details can be provided.

Funding 18 in total, including conditional, spending £1.15m total, had £1.3m to spend, so £150k left will be rolled over.

## Awards made:

| **Priority** | **Title** | **Div.** | **PI** | **Award** | **Source** |
| --- | --- | --- | --- | --- | --- |
| **1** | Evaluation of the efficacy of an mRNA-based multi-antigen vaccine against tuberculosis (TB) disease in guinea pigs. | MSD | Stylianou, Elena | £85,000.00 | MRC IAA (£42,500.00)  Wellcome (£42,500.00) |
| **2** | Developing a novel therapeutic for treating heart failure | MSD | Nanchahal, Jagdeep | £84,811.10 | MRC IAA (£42,405.55)  Wellcome (£42,405.55) |
| **3** | Developing the OxNNet Toolkit to facilitate estimation of in-utero fetal brain perfusion in real time | MSD | Collins, Sally | £61,650.87 | MRC IAA (£30,825.44)  Wellcome (£30,825.44) |
| **4** | Development of mechanotherapeutics for cardiometabolic diseases | MSD | Tzima, Ellie | £89,337.36 | MRC IAA (£42,865.20)  Wellcome (£42,000.00) |
| **5** | SMIITE: A Soluble MHC-II restricted TCR Engager To Treat TP53, K-RAS and APC Mutant Colorectal Cancer | MSD | Vyas, Paresh | £51,466.50 | MRC IAA (£25,733.25)  Wellcome (£25,733.25) |
| **6** | FSL Clinical: Automated brain imaging analysis to support the diagnosis of psychosis | MSD | Clarke, William | £83,774.27 | MRC IAA (£41,887.14)  Wellcome (£41,887.14) |
| **7** | Bifunctional molecules to combat antimicrobial resistance | MSD | Lanyon-Hogg, Thomas | £43,233.80 | MRC IAA (£28,008.46)  Wellcome (£15,225.34) |
| **8** | A novel metabolic agent for the treatment of chronic inflammatory diseases | MSD | Williams, Richard | £54,476.00 | MRC IAA (£27,238.00)  Wellcome (£27,238.00) |
| **9** | Development of novel therapeutics for T cell malignancies | MSD | Ogg, Graham | £85,000.00 | MRC IAA (£41,500.00)  BRC (£43,500.00) |
| **10** | Foundational Large Language Models for Supporting Primary Care | MSD | Clifton, Lei | £81,823.17 | MRC IAA (£25,911.61)  Wellcome (£24,000.00) |
| **11** | Quick and Easy Scrub Typhus Diagnostics (QuEST) | MSD | Perrone, Carlo | £44,365.00 | MRC IAA (£22,344.00)  Wellcome (£22,021.00) |

| **12** | Development of new small molecules as regenerative medicines for Duchenne Muscular Dystrophy | MSD | Russell, Angela | £63,700.03 | MRC IAA (£25,700.03)  Wellcome (£38,000.01) |
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| **13** | Retinal gene therapy in a mouse model of USH2A-associated retinitis pigmentosa using DNA minicircles as a novel vector for delivery of large transgenes | MSD | MacLaren, Robert | £84,288.85 (£58,288.85)\* | MRC IAA (£36,288.85)  Wellcome (£22,000.00) |
| **14** | The use of stimulation induced evoked potentials for closed-loop DBS programming and titration | MSD | Tan, Huiling | £74,353.98 | MRC IAA (£30,853.98)  BRC (£43,500.00) |
| **15** | Preparing optimised primaquine granules to scale up for malaria elimination | MSD | Taylor, Walter | £85,000.00 | MRC IAA (£41,400.00)  Wellcome (£43,600.00) |
| **16** | Developing a lateral flow test for early detection of intravascular haemolysis using urinary carbonic anhydrase 1 excretion as its real-time biomarker | MSD | Swietach, Pawel | £83,521.60 | MRC IAA (£43,521.60)  Wellcome (£40,000.00) |
| **17** | GLUT1 receptor-mediated therapeutic oligonucleotide delivery across the blood-brain barrier | MSD | Frommer, Jennifer | £50,000 | MRC IAA (£25,000.00)  Wellcome (£25,000.00) |
| **18** | Can the anti-cancer therapeutic compound NBS037 prevent or reduce metastatic burden? | MSD | Morten, Karl | £85,000 | MRC IAA (£42,500.00)  Wellcome (£42,500.00) |

\*Note on project priority 13, Robert MacLaren - The panel have agreed to fund on the condition that the £26k for the electroporation kit is removed. This is a duplication cost with the JFF fund. P