The International Alliance for Cancer Early Detection (ACED): Strategy and Opportunities Overview

Overarching Vision

To transform the field of early detection of cancer research through establishing an international alliance of world-leading, multidisciplinary cancer early detection locations.

Purpose of ACED

The Alliance intends to unite fragmented and siloed research and infrastructure by connecting the top US and UK early detection cancer centres, bringing together thought leaders to raise the profile of the field, create new collaborations and ideas to tackle the biggest problems in early detection at the appropriate scale.

1. The International Alliance for Cancer Early Detection (ACED)

ACED is a partnership between Cancer Research UK (CRUK), the Canary Center at Stanford University, the University of Cambridge, the Knight Cancer Institute at the Oregon Heath and Sciences University (OHSU), University College London (UCL) and the University of Manchester. The Directors sitting on ACED's governing Alliance Executive Board (AEB) are:

- Dr Iain Foulkes, CRUK – *interim AEB member*
- Professor Utkan Demirci, University of Stanford
- Professor Rebecca Fitzgerald, University of Cambridge
- Professor Sadik Esener, OHSU
- Professor Mark Emberton, UCL
- Professor Rob Bristow, University of Manchester

Over the first five years of ACED's existence, Cancer Research UK has committed up to £40m for research activities and infrastructure to support the Alliance and the Canary Center and Knight Institute have each committed up to $10m. Please see Appendix 3 for the 'Guiding Principles' of the Alliance.

2. Getting Involved

This is your opportunity to be part of a globally unique early detection (EDx) virtual institute where, as a member, you will have access to research funding and infrastructure which will enable new ways of taking on the challenge of EDx through knowledge exchange and collaborative research.

Key opportunities for **YOU** as an ACED member:

- Access collaborative research funding to work with researchers at other ACED Member Centres
- Access funding for students and early-career fellows, and for visits to other ACED Member Centres
- Engage with diverse multidisciplinary experts across five world-leading centres in collaborative research, infrastructure access and development, thought leadership pieces, etc.
- Feed into the AEB with transformative new ideas for how to shape the Alliance
- Participate in networking/brainstorming events with colleagues across the Alliance, both in person and virtually:
  - Working group meetings
  - In-person networking events
  - Forthcoming online community platform and virtual workshops

For more information on how to get involved, please speak with the Director or Programme Manager at your Member Centre *(see Appendix 2).*

3. Key Aims of the Alliance

The Alliance aims to:

- **Be an international hub for the EDx community**, raising visibility of the field, setting the standard for excellence and acting as global thought leaders.
- **Activate the best research** by uniting world-leaders in the field through a prestigious, high-profile alliance.
- **Set and execute a strategy for EDx research,** setting the tone for the Alliance and the wider field, and building on and complementing existing external successful initiatives.
- **Facilitate and drive knowledge, technology and skills exchange** between sites, to capitalise on complementary expertise, tools and technologies, reduce redundancy of effort and accelerate progress.
- **Train the brightest minds and build capacity** in the field, creating a new generation of EDx scientists.
- **Develop, pool and harmonise complex, siloed infrastructure** (e.g. cohorts, samples, data warehouses and analytic platforms) to tackle problems at greater scale.
- **Provide a portal for industry access** to world-leading EDx expertise, stimulating industry engagement with EDx and accelerating translation.
- **Create a clear platform and globally unique proposition** to generate philanthropic fundraising to support long-term sustainability.

4. ACED Scientific Strategy

The ACED AEB has developed three broad, overarching strategic themes, where world-leading expertise is located across the Alliance Member Centres, and where the Alliance will be uniquely positioned to drive and accelerate progress towards the early detection of cancer:

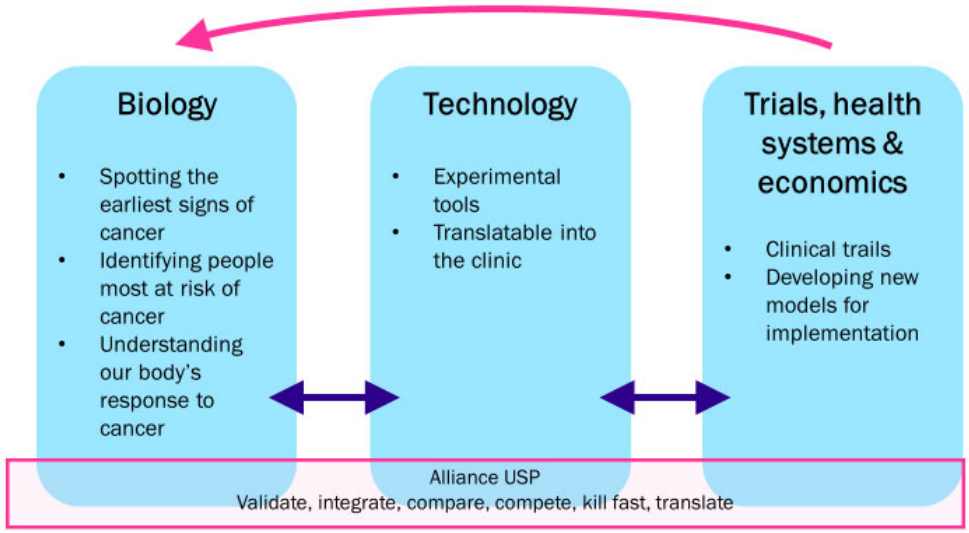

Figure 1: ACED Strategic Themes

Biology: Fundamental research into mechanisms of cancer development, including individual susceptibility/risk, in order to inform EDx; the Alliance will be at the forefront of exploring and understanding early and pre- cancer biology in order to detect and intercept cancers early, and to better predict future disease trajectory to consequential versus inconsequential disease. The Alliance will focus on the EDx of primary disease.

Technology innovation as an enabler: The Alliance will lead the field in developing and validating technologies at the cutting edge of EDx. This will include innovation in new tools to probe biological mechanisms and enable research, plus translatable technologies to develop as clinical EDx approaches.

Trialling and translating EDx technologies to practice: The Alliance will set new standards for how to evaluate the performance characteristics, clinical effectiveness and cost effectiveness of EDx approaches and technologies. The will include innovation and best practice in EDx trial methodology, health systems and health economics research and will include facilities for first-into-human studies.

Alliance USP: ACED will use its unique convergence of its five Member Centres' expertise to externally validate emerging markers and technologies, to compare and compete such approaches to find the "best", integrate multiple approaches where appropriate, and to accelerate the rate at which new EDx approaches are either dropped due to poor performance, or are translated to clinical benefit.

Alliance Research Themes

Within the three overarching strategic themes described above, ACED will organise itself around six ***research themes***. The below diagram illustrates how these six research and scientific infrastructural themes map onto the three overarching strategic themes described (shown as the three blue pillars), and how knowledge and innovation will flow between them.

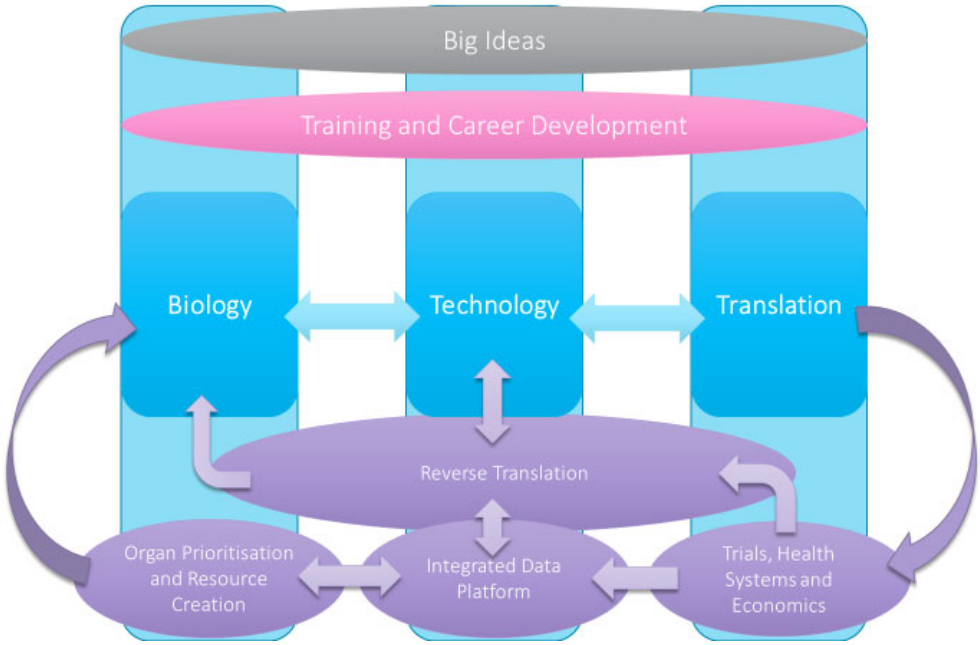

Figure 2: ACED Research Themes

Alliance 'Big Ideas': The critical mass of leading researchers in the Alliance allows for the generation of extraordinary new ideas for tackling the most challenging and complex problems in cancer early detection. 'Big Ideas' will be transformative and high-risk; it is expected that major programmatic ACED funding will be dedicated to these 'Big Ideas', and could include (but are not limited to) areas of interest such as:

- *A tissue biopsy-free EDx approach*: using advanced imaging and distal samples taken from urine, saliva, blood, mucosal swabs or exhaled breath analysis, etc. could make more invasive biopsies obsolete. This would make EDx "population-friendly" with reduced anxiety and morbidity and, therefore improved compliance for serial screens.

- *Proximal sampling approaches*: tissues or fluid proximal to the early lesions (e.g. urine for bladder cancer, saliva from head and neck cancers, pancreatic cyst fluid) may be useful when the biopsy of the lesion itself is difficult, the lesion is too small to biopsy and/or insufficient lesion material has reached the circulation to be detectable.
- *Nanodetection and nanomedicine*: the use of "bots" to detect and treat early lesions.

Alliance researchers will have the opportunity to be a part of the collaborative teams generating, defining and exploring these ideas, and submitting new ideas via Alliance Working Groups.

Integrated data platform: Most early detection clinical data sets are limited in scope, poorly integrated with emergent data and unavailable for exploitation by potential users; the Alliance will address this with an Integrated Data Platform (IDP). Given its membership across five institutions and geographies, the Alliance is in a unique position to bring datasets from many existing clinical and research cohorts into one cross-analysable platform for the first time. The platform will seek to integrate across various data types (data from screening tests, primary and secondary care health records, diagnostic imaging, histopathology slides, ctDNA data etc.) and will generate a globally unique resource for Alliance members to access and study.

Organ prioritisation: In order to provide the necessary critical mass to make an impact, the Alliance will need to prioritise the cancer types or organs-of-origin it will focus on initially. Going through a process of systematic prioritisation of cancer types of focus (based on a system of defined criteria) will lead to the best investment of time, resources, and expertise the Alliance has to offer, and the greatest potential for making a significant clinical impact.

Reverse translation from samples/data to biology/technology: The understanding that can be derived from measurements and data obtained from primary human samples and patients by the Alliance will provide exciting opportunities to reverse-translate and glean further understanding of biology (underpinning detection and prognosis), generate new models, and develop novel technologies (as tools to probe biology and as approaches which are translatable to the clinic).

Trials, health systems and economics: While progress in EDx basic research has yielded some innovative technologies and approaches to detect and risk stratify cancer, a focused and coordinated effort to evaluate these strategies in the clinic is lacking. To bridge the gap between fundamental research and late stage trials, ACED will provide the infrastructure and specialist expertise required to efficiently translate earlier cancer detection and intervention approaches into patient benefit. The Alliance will innovate in the methodologies for most efficiently testing the cost and clinical effectiveness of EDx approaches.

Training and career development - ACED has an opportunity and a responsibility to establish the EDx field to be attractive to the best and brightest researchers, and to support their career development in new ways. The Alliance seeks to strengthen and expand the EDx by engaging with researchers early-on in their career and promoting EDx as a worthwhile research focus with ample opportunities for scientific growth and breakthroughs for professional success. ACED will provide novel training and career development funding and other opportunities to do multidisciplinary training in a new way through international collaboration, capitalising on the strengths across the five sites.

5. ACED Working Groups

While the high-level vision outlined in this document has been developed by the AEB, the Alliance Working Groups (WGs) will be the engine of strategy development for ACED. All ACED members will have the opportunity to engage with and input into these WGs. At this time, seven WGs have been established to develop strategy, collaborative research concepts, infrastructural investments and thought leadership publications. Their activities align to the ACED strategic and research themes described above. Each WG includes representatives from all five Member Centres, who is charged with being a conduit of information between your Member Centre and the WG/AEB. The initial seven WGs are:

- "Big Idea" Proximal Sampling Approaches WG
- "Big Idea" Tissue Biopsy-Free WG
- Integrated Data Platform WG
- Organ Prioritisation WG
- Lung WG *(initial exemplar to map Alliance capabilities and explore prioritisation)*
- Prostate WG *(initial exemplar to map Alliance capabilities and explore prioritisation)*
- Training and Career Development WG

Should you wish to input into these WGs, please contact your local Programme Manager (Appendix 2).

6. Funding

Funding will be available to Alliance members at various levels, from small seed funding awards through to large programmatic funding. All projects funded by the Alliance will involve at least two Member Centres. Transatlantic collaboration is encouraged but not mandatory. The following opportunities are available:

- **Pilot funding**: up to £200,000 (~$250,000) for up to 1 year
  The ACED Pilot Awards fund exceptional science, supporting innovative, novel approaches in how and when cancer is detected through collaborative research with ACED Members.

- **Skills Exchange and Development Award**: up to £40,000 (~$50,000) for up to 4 months
  Flexible funding for researchers of any career stage to visit another Alliance Centre or Centres to learn a new technique or develop a particular skillset. Funding covers travel, accommodation and training costs for the individual. These awards will also aim to seed future cross-ACED collaborative research projects.

The following opportunities will be available from 2020 onwards:

- **Project funding**: from £200,000 to £800,000 (~$250,000 to $1 million) for up to 3 years
  Funding for transformative research projects to drive innovation in how and when cancer is detected, accelerating progress towards the Alliance's strategic aims. Proposals may be at various stages of maturity dependent on technology readiness, novelty of the paradigm under investigation and availability of supporting data. Proposals should be composed and costed commensurately.
- **Programmatic funding**: >£800k (>$1 million)
  Over the first 1-2 years of the Alliance, the AEB will develop several large, engineered/top-down major research programmes, with input from the WGs. Such large, strategic programmes will predominantly involve all five Member Centres.
- **ACED PhD Scholars: details TBD**
  These ACED-branded PhD studentships will each be hosted by one ACED Member Centre but with time spent at other Member Centres. They will be supported by a range of unique Alliance training and support opportunities delivered across the five sites.
- **ACED Fellows: details TBD**
  Career development awards to support the progression of promising early-career investigators towards research independence, hosted by one Member Centre but with time spent at, and in collaboration with, another Member Centre. Fellows will be supported through the Alliance to experience multidisciplinary, collaborative research environments and develop into strong leaders who, in turn, will further expand and promote the EDx field.

As of November 2019, the following opportunities are available:

Pilot funding, Skills Exchange and Development Awards, Expressions of Interest for Project funding. Proposals are welcome across the entire scientific remit of the Alliance – see Appendix 1

Appendix 1: ACED Scientific Remit

ACED will engage in EDx research, defined as that which seeks to enable the primary detection of cancer, or pre-cancerous states, at the earliest possible time point at which an intervention might be made. It includes discovery and validation of the signatures of early (and pre-) cancer, and development and translation of the technologies to enable such discovery and validation. These signatures may detect and also underpin prognosis, stratification, treatment decision, prediction of response to therapy and/or prevention of cancer. This involves:

Biological research underpinning early detection and biomarker discovery and validation, including but not limited to:

- Basic cellular and molecular science around the earliest transformational events pushing a cell from normal to at-risk to dysregulated to cancerous, thereby suggesting potential early detection markers to be explored (including understanding of cancer cells' interaction with the local and immune microenvironment and the discovery of EDx signatures pertaining to this)
- 'Omics for early detection: high-throughput, high-dimensional data research in markers for early detection, including proteomics, metabolomics, lipidomics, genomics, epigenomics, transcriptomics
- Basic biology and detection of circulating cellular and nucleic acid markers for early detection of cancer or pre-disease (e.g. ctDNA, CTCs, exosomes, RNAs, etc.)
- Studies may include the use of model systems, such as model organisms, cell lines, organoids and xenografts, or primary human samples

Human-based EDx discovery research including but not limited to:

- Biomarker discovery and validation in early stage disease (and pre-cancerous state) patients
- Biomarker discovery and validation in healthy volunteers
- Exploitation of existing cohorts and biobanks for discovery research and technology development in an early detection context

Stratification of populations by risk to identify and exploit high-risk groups as populations for EDx research, and as appropriate clinical contexts for development of novel detection technologies

- Use of the tools, methods and insights of population science, epidemiology and risk assessment through collaborative research with behavioural scientists, psychologists and primary care physicians to inform the above.

Data and computation-driven approaches to EDx, including but not limited to:

- Biomedical and health informatics: computational high-dimensional data analytics for interpretation of potential EDx marker profiles; analysis and integration of (multimodal) data arising from e.g. genomics, proteomics, imaging, e-health records, patient/public-derived data (personal activity monitors, etc.)
- Computational and systems biology: computational and mathematical modelling of complex networks and systems to understand normal, pre-cancer and early cancer biology. Modelling of the interaction within and between complex biological systems to facilitate EDx and prediction of implications of markers (e.g. distinguishing lethal from dormant disease).

Development and utilisation of preclinical EDx model systems (e.g. human cellular and organoid models, xenograft, animal model) to recapitulate early cancer and precancerous states, including but not limited to:

- Creation and characterisation of new model systems

- Use of model systems to probe and understand early events leading from normal cellular function through to cancer
- Use of model systems to identify potential EDx markers for future clinical validation
- Use of model systems as platforms for development of EDx technologies

EDx technology development – exploratory and translational research, including but not limited to:

- Imaging: progressive research into advanced imaging technologies for cancer detection. Novel modalities, novel probes, novel contrast agents, novel imaging methodologies (of existing modalities) etc.
- Circulating marker detection technology: enhancement of sensitivity/specificity of detection technologies for ultra-low concentration circulating markers (e.g. cells, DNA, proteins, exosomes, metabolites, etc.)
- Advanced detection technologies (nanotech, photonics, synthetic markers, etc.): engineering and physical science to enable novel methods of detection of very low-concentration markers

Translational and clinical EDx research: experimental work in patients and healthy volunteers around development and validation of EDx approaches and technologies

Appendix 2: Key Contacts

Affiliation	Name	Role	Contact Information
Cancer Research UK	Karolin Kroese	ACED Programme Manager	E: Karolin.Kroese@cancer.org.uk
Cambridge	Wendy Alderton	Programme Manager	wa266@cam.ac.uk
University College London	Daniel Kelberman	Programme Manager	d.kelberman@ucl.ac.uk
OHSU	Erin Watson	Programme Manager	watsoner@ohsu.edu
Stanford	Ryan Spitler	Programme Manager	rspitler@stanford.edu
Manchester	Martin Bone	Programme Manager	martin.bone@manchester.ac.uk
Manchester	Ellena Badrick	Interim Programme Manager	ellena.badrick@manchester.ac.uk

Appendix 3: Key Guiding Principles of the Alliance

The following outlines key Guiding Principles of the Alliance:

Vision

1. Alliance Member Centres will endeavour that their participation enables the scientific community to support progress in early detection research, ultimately leading to increased benefit for patients
2. Alliance Member Centres commit to look for ways to break down barriers and silos in cancer early detection research
3. Alliance Member Centres commit to developing and pushing capacity in the early detection field
4. Alliance Member Centres will work together to define the research priorities for the Alliance

Contribution & Collaboration

5. Alliance Member Centres agree to bring unique research, expertise and resources to the Alliance

6. Each Alliance Member Centre agrees to work collaboratively and share complementary expertise with other Alliance Member Centres, and will be willing to work in partnership across the Alliance and ultimately to support the wider EDx community (while recognising that relevant EDx research will still take place within individual Member Centres, which will not be constrained by EDx research under the Alliance)
7. Alliance Member Centres will share data across the Alliance, where possible, and for work funded through the Alliance, there is an expectation that data generated will be openly shared across the Alliance.
8. Alliance Member Centres will, to the extent permissible, share outputs, resources and tools across the Alliance
9. Alliance Member Centres will commit scientific and intellectual resources to the Alliance for effective implementation of Alliance directives
10. Alliance Member Centres will commit to their operational delivery staff helping to implement the vision of the Alliance and delivering Alliance activity locally. Alliance Member Centres will commit to support training, capacity building and career development opportunities for current and future generations of early career researchers in EDx

Communication

11. Timely communication and openness between Alliance Member Centres will be a top priority to ensure momentum and effective implementation for the Alliance
12. Alliance Member Centres will actively communicate Alliance aims and opportunities to their scientific communities, increasing the visibility for EDx research
13. Alliance Member Centres will appropriately recognize the Alliance and its participants in all relevant communications

External engagement

14. Alliance Member Centres will explore how industry can best be engaged in the Alliance to ensure effective translation of research and increase investment in the Alliance
15. Alliance Member Centres will explore the opportunity to generate philanthropic revenue for the Alliance
16. Alliance Member Centres will be cognizant of the vision of a self-sustaining network, by exploring other sources of funding where possible
17. Alliance Member Centres will be cognisant of the strengths of existing centres of excellence, infrastructure and networks beyond the Alliance, in the US, UK and globally; the Alliance will seek to build on and synergise with these external strengths
18. Alliance Member Centres will seek to be thought leaders, setting and driving the EDx research agenda and raising the visibility of the field globally. The Alliance will engage with and seek to positively influence researchers, research institutions, industry, healthcare providers and payers
19. Alliance Member Centres will seek ways to appropriately engage patients and the public in the planning and execution of research and in communications and positioning around EDx research