Name	KATHY NIAKAN
Position	Group Leader (2nd 6)
Year joined *(Crick or founder institute)*	2013

Career History

2000-2005: PhD, Department of Human Genetics, University of California, Los Angeles, (UCLA) USA
2005-2009: Postdoctoral fellow, Department of Molecular and Cellular Biology, Harvard University, USA
2009-2013: Next Generation Research Fellowship, Centre for Trophoblast Research, University of Cambridge, UK

Major Awards, Honours and Prizes

2019: Blavatnik Awards UK Finalist in Life Sciences
2019: Honorary Life Fellowship Galton Institute
2018: HFEA original licence is part of the permanent collection at the Science Museum, London
2016-2018: Exhibition of equipment and instruments from our lab at the “Who Am I?” exhibit at the Science Museum, London
2016: Nature Journal “Ones to Watch”
2007: Distinction in Teaching Award, Harvard University, Derek Bok Centre for Teaching
2004-2005: Chancellor’s Dissertation Year Fellowship, UCLA
2002-2003: National Institutes of Health Pre-doctoral Training Grant, UCLA
2000-2004: Paul D. Boyer Fellowship, UCLA
1999: Mary Gates Endowment for Students Research Scholarship, University of Washington

Membership of external committees, editorial boards, review panels, SABs etc.

2018-present: Member of the Wellcome Trust Cell and Developmental Biology Expert Review Group.
2019-present: Member of the International Society for Stem Cell Research Working Group tasked with providing international guidelines on human embryo research, including *in vitro* embryo models (blastoids/gastruloids), the 14-day rule, and *in vitro* derived gametogenesis.
2020-present: Member of the editorial advisory board of *Cell*.

Lab Name	***Human Embryo and Stem Cell Laboratory***

Research programme and achievements

The aim of research in my laboratory is to provide molecular insights into how early human development is controlled. The mechanisms that regulate early cell lineage decisions in human development remain poorly understood, despite their fundamental biological importance and wide-reaching clinical implications for understanding infertility, miscarriages, developmental disorders and therapeutic applications of stem cells. My laboratory has pioneered approaches to investigate the function of genes that regulate human preimplantation embryo development. During the quinquennium, we have uncovered a mechanism underlying the first lineage decision in human embryogenesis; discovered gene regulatory networks specific to human embryos, which are not found in mouse embryos; and identified mechanisms that are evolutionarily conserved across mammals.

These discoveries validate the need to study human embryos directly. By integrating signalling insights gained from transcriptomic analysis of human blastocysts, we have defined human embryonic stem cell culture conditions that more closely recapitulate the embryonic niche. The foundation of knowledge we have generated will be informative to further improve *ex vivo* models to better understand human biology. Furthermore, by applying the knowledge we gained from dissecting the molecular programmes in the developing embryo, we have identified signalling pathways and transcription factors that mediate a cell fate switch from a pluripotent embryonic stem cell (ESC) to yolk sac or placental progenitor cells. We have demonstrated that these cellular models are tractable systems for molecular genetic analysis and in the future anticipate that they will be informative to understand yolk sac or placental disease.

Our laboratory has contributed to engineering optimised models of early implantation, which has revealed a degree of self-organisation in the absence of maternal tissue. We also generated extensive pre-clinical data that were part of the evidence used to support changes in UK law regulating mitochondrial replacement therapy, a novel reproductive technology to prevent fatal inherited mitochondrial diseases. In all, we have established an international reputation for our expertise in early human development.

Future plans:
Our future plans are to transform our understanding of the molecular mechanisms that control early human development. We seek to uncover when and how human embryonic epiblast cells are established and maintained, and to understand the molecular mechanisms that distinguish these pluripotent cells from extra-embryonic cells during embryogenesis. We will further develop pioneering methods to investigate gene function during human embryogenesis using CRISPR-Cas9-mediated genome editing, TRIM-Away protein depletion, constitutively active and kinase dead variants of proteins and small molecule inhibitors and activators. These approaches will enable us to directly test the function of genes involved in Hippo and TGFβ signalling, and key transcription factors downstream of these pathways, which we hypothesise are involved in the first and second cell fate decisions, respectively. Altogether, we expect this programme to make significant advances in our understanding of the molecular programmes that shape early human embryogenesis, with the potential to provide fundamental insights and to drive clinical translation.

Research outputs

Gerri C., McCarthy A., Alanis-Lobato G., Demtschenko A., Bruneau A., Loubersac S., Fogarty N.M.E., Hampshire D., Elder K., Snell P., Christie L., David L., Van de Velde H., Fouladi-Nashta A.A. and Niakan K.K. (2020) *Initiation of a conserved trophectoderm program in human, cow and mouse embryos*. Nature, 587(7834):443-447. DOI: 10.1038/s41586-020-2759-x

We discovered that the mechanism underlying the first lineage decision in human embryos is mediated via cell-cell contact, triggering a cascade of broadly evolutionarily conserved molecular events that initiates a switch to a placental progenitor programme. We believe that our study will have clinical impact given that the timing of this decision coincides with the stage when most human embryos arrest.

Wamaitha S.E., Grybel K.J., Alanis-Lobato G., Gerri C., Ogushi S., Mahadevaiah S.K., Healy L., Lea R.A., Molina-Arcas M., Elder K., Snell P., Christie L., Downward J., Turner J.M.A. and Niakan K.K. (2020*) IGF1-mediated human embryonic stem cell self-renewal recapitulates the embryonic niche*. Nature Communications, 11: 764. DOI: 10.1038/s41467-020-14629-x
In this work we mined this database to refine hESC culture conditions. These data will be a powerful resource for the community and will lead to changes in how hESCs are cultured in the future. Building on these data, we demonstrated that IGF1-receptor/PI3K/AKT, but not FGF receptor, signalling is required for hESC self-renewal. We built a searchable website that includes a compendium of human embryo gene expression analysis and compiled a list of all possible ligand and receptor interactions.

Fogarty, N.M.E., McCarthy, A., Snijders, K.E., Powell, B.E., Kubikova, N., Blakeley, P., Lea, R., Elder, K., Wamaitha, S.E., Kim, D., Maciulyte, V., Kleinjung, J., Kim, J.-S., Wells, D., Vallier, L., Bertero, A., Turner, J.M.A. and Niakan K.K. (2017) *Genome editing reveals a role for OCT4 in human embryogenesis*. Nature, 550(7674): 67-73. DOI: 10.1038/nature24033
The first demonstration of the utility of CRISPR–Cas9-mediated genome editing for investigating gene function in the context of human embryonic development. We revealed a distinct role for the developmental regulator OCT4 in human versus mouse development.

Hyslop L.A., Blakeley P., Craven L., Richardson J., Fogarty N.M., Fragouli E., Lamb M., Wamaitha S.E., Prathalingam N., Zhang Q., O'Keefe H., Takeda Y., Arizzi L., Alfarawati S., Tuppen H.A., Irving L., Kalleas D., Choudhary M., Wells D., Murdoch A.P., Turnbull D.M., Niakan K.K. and Herbert M. (2016) *Towards clinical application of pronuclear transfer to prevent mitochondrial DNA disease*. Nature, 534(7607): 383-386. DOI: 10.1038/nature18303
A preclinical study on the use of pronuclear transplantation for mitochondrial replacement therapy. For this study, my laboratory performed transcriptional comparisons of cells, derived human embryonic stem cells and performed molecular characterisation.

Wamaitha S.E., del Valle I., Cho L.T., Wei Y., Fogarty N.M.E., Blakeley P., Sherwood R.I., Ji H. and Niakan K.K. (2015) *Gata6 potently initiates reprogramming of pluripotent and differentiated cells to extraembryonic endoderm stem cells*. Genes and Development, 29(12): 1239-1255. DOI: 10.1101/gad.257071.114
Using genomics, genome-wide transcriptional and chromatin immunoprecipitation analyses, we discovered that the transcription factor Gata6 is able to rapidly and directly inhibit core and peripheral genes within the pluripotency regulatory network, as well as directly activate an extraembryonic endoderm program to facilitate cellular reprogramming. The cell lines we engineered and datasets we generated have been used by several international laboratories.