OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Rachel Abbotts

eRA COMMONS USER NAME (credential, e.g., agency login): RABBOTTS

POSITION TITLE: Research Associate

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE(if applicable) | Completion DateMM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| University of Leeds, UK | BSc  | 07/2003 | Human Genetics |
| University of Leeds, UK | MBChB | 07/2006 | Medicine |
| University of Manchester, UK |  | 08/2008 | Academic Foundation Programme |
| University of Nottingham, UK |  | 12/2010 | Academic Clinical Fellow in Medical Oncology |
| University of Nottingham, UK | PhD | 03/2014 | Medical Oncology |
| National Institute on Aging, Baltimore MD |  | 05/2017 | Postdoctoral Fellow |
| University of Maryland Baltimore MD |  | 10/2019 | Postdoctoral Fellow |
| University of Maryland Baltimore MD |  | Present | Research Associate |

**A. Personal Statement
During my research career, I have focused on the role of DNA repair in human health and disease, including cancer. After completed my medical degree, I focused on developing an academic career through a structured clinical academic training track in the United Kingdom. During this time, I completed core medical training (equivalent to residency) in adult internal medicine and embarked on a fellowship in medical oncology that included experience in conducting and contributing to both local early stage and international multi-site clinical trials. I joined the laboratory of Prof. Srinivasan Madhusudan at the University of Nottingham, where I conducted research on development of inhibitors of the key base excision repair protein APE1, and applied these to PTEN-deficient melanomas in a synthetic lethality approach. Preliminary experimental data led to the successful application to the Medical Research Council Clinical Research Training Fellowship program, providing salary support and direct costs for a three-year period that led to the award of a PhD from the University of Nottingham. I subsequently elected to continue on a research career track, joining the laboratory of Dr. David Wilson III at the National Institute on Aging, where my work focused on the role of base excision repair in the maintenance of mitochondrial health in skeletal muscle. This work, supported by competitive NIH intramural funding, received the NIH Fellows Award for Research Excellence.**

**In my current role in the laboratory of Dr. Feyruz Rassool at the University of Maryland Baltimore, I am investigating the mechanisms underpinning the therapeutic efficacy of a novel combination regimen in non-small cell lung and other cancers. My work, recently published in *PNAS*, has demonstrated that epigenetic modulation by DNMT inhibitors (DNMTi) induce a defect in double strand break repair that sensitizes cancer cells to PARP inhibitors and radiation therapy. Ongoing studies now link this DNMTi-induced repair defect with induction of an interferon-stimulated immune response that may modulate response to immune checkpoint therapy. My 10 years’ experience in the field of DNA repair research, including expertise in widely varied experimental techniques, along with my increasing role in project development during this period, have provided me with the necessary experience to successfully contribute to the proposed research project.**

**B. Positions and Honors
Positions and Employment**

**2006-2008 Academic Foundation Trainee, University Hospitals of South Manchester, UK**

**2008-2013 Academic Clinical Fellow, Nottingham University Hospitals, UK**

**2013-2017 Postdoctoral Fellow, National Institute on Aging, Baltimore MD**

**2017-2019 Postdoctoral Fellow, University of Maryland Baltimore, Baltimore MD**

**2019-Present Research Associate, University of Maryland Baltimore, Baltimore MD**

**Other Experience and Professional Memberships**

**2019 Assistant Course Director, Graduate Program in Life Sciences Cancer Biology: Research to Clinic, University of Maryland Baltimore**

**2019 Associate Member, American Association of Cancer Research**

**2017-2019 Postdoctoral Advisory Committee, Member At Large, University of Maryland Baltimore**

**2018 Career Advisory Group, University of Maryland Baltimore**

**2017 Graduate Program in Life Sciences Award Committee Member, UMB**

**2008 Membership of the Royal College of Physicians, London UK**

**Honors**

**2017 NIH Fellows Award for Research Excellence, Bethesda MD**

**2012 NCRI Student Prize, NCRI Annual Conference**

**2010 Attendance Scholarship, AACR/ASCO Methods in Clinical Cancer Research**

**C. Contributions to Science**

**1. Graduate career:** My graduate research at the University of Nottingham focused upon modulation of the base excision DNA repair protein APE1 as a therapeutic target in melanoma. I expanded upon the drug development program in place in the laboratory of Dr. Srinivasan Madhusudan to screen potential small molecule inhibitors of APE1 endonuclease activity using a radionuclide incision assay. I assessed the most promising inhibitory compounds for synthetic lethality in PTEN-deficient cells, which had recently emerged as potential marker for a double strand break repair defect. This work was supported by a successful application to a nationally competitive Medical Research Council Clinical Research Training Fellowship, and was awarded a student prize at the National Cancer Research Institute (NCRI) Annual Conference in 2012. The work produced a first author paper, three first author review articles, and co-authorship on a further eight papers.

1. **Abbotts R,** Jewell R, Nsengimana J, Maloney DJ, Simeonov A, Seedhouse C, Elliott F, Laye J, Walker C, Jadhav A, Grabowska A, Ball G, Patel PM, Newton-Bishop J, Wilson DM 3rd, Madhusudan S. Targeting human apurinic/apyrimidinic endonuclease 1 (APE1) in phosphatase and tensin homolog (PTEN) deficient melanoma cells for personalized therapy. *Oncotarget* 2014; 5(10): 3273-86.
2. **Abbotts R**, Madhusudan S. Human AP endonuclease 1 (APE1): from mechanistic insights to druggable target in cancer. *Cancer Treatment Reviews* 2010; 36(5): 425-435
3. **Role of XRCC1 in skeletal muscle maintenance:** My postdoctoral research at the National Institute on Aging focused upon the role of base excision repair in skeletal muscle development and aging. In developing a new area of research for the Wilson laboratory, I supervised a breeding program to establish skeletal muscle-specific XRCC1 knockout mice, and developed isogenic cell line systems (in immortalized mouse myoblasts, and primary human and mouse skeletal muscle cells). I established lines of investigation to assess the role of XRCC1 in a) skeletal muscle differentiation; and b) the maintenance of mitochondrial health via NAD+/SIRT1 signaling. This work was supported by successful application to the NIA intra-laboratory intramural grant program (PI David M Wilson III), including second year renewal following annual review at which I was primary presenter (due to Dr. Wilson’s research secondment in Europe). For this work, I was awarded the NIH Fellows Award in Research Excellence in 2017.
4. **Abbotts R**, Golato T, Wilson DM 3rd. Role of DNA repair in carcinogenesis and cancer therapeutics. Invited review, under submission to *Encyclopedia of Cancer, Third Edition.* Amsterdam, The Netherlands: Elsevier.
5. **Abbotts R** and Wilson DM 3rd. Coordination of DNA Single Strand Break Repair. *Free Radical Biology & Medicine* 2017: 107:228-244.
6. **Therapeutic induction of DNA repair defects in NSCLC using epigenetic agents:** My current research at the University of Maryland Baltimore utilizes inhibitors of DNA methyltransferase (DNMTi) in non-small cell lung cancer (NSCLC) models to induce defects in DNA repair, mediated by reduced expression of key double strand break repair genes. These include factors involved in homologous recombination repair, leading to sensitization to PARP inhibitors, and in non-homologous end joining, producing radiosensitization. Ongoing projects aim to elucidate the mechanism by which these repair defects are produced, including refining our recent novel link to a DNMTi-induced interferon-stimulated immune response, and to translate these findings to a clinical trial in NSCLC.
7. **Abbotts R**, Topper M, Biondi C, Fontaine D, Goswami R, Stojanovic L, Choi EY, McLaughlin L, Xia L, Mahmood J, Lapidus RG, Baylin SB, Rassool FV. DNA methyltransferase inhibitors induce a BRCAness phenotype that sensitizes NSCLC to PARP inhibitor and ionizing radiation. *Proc Natl Acad Sci U S A* 2019 Oct 7. pii: 201903765. doi: 10.1073/pnas.1903765116.

**Complete List of Published Work in MyBibliography:**

<https://www.ncbi.nlm.nih.gov/myncbi/rachel.abbotts.2/bibliography/public/>

**D. Current Research Support**

**American Cancer Society Institution Research Grant Institution PI: S. Martin; Project PI: R Abbotts**

**“Targeting DNA repair defects by induced by immune signaling in NSCLC”**

**Goal: Elucidate mechanistic basis of efficacy of DNMTi+PARPi combination in lung cancer, focusing on interaction between immune signaling, c-MYC suppression, and DNA repair defect induction. My current focus is determining the interaction between c-MYC and DNA repair factors including FANCD2 and Ku70 by ChIP/co-IP, and validation in CRISPR-engineered cell lines currently under development.**

**Role: Principal Investigator**

**Effort: 0%**

**Adelson Medical Research Foundation PI: S. Baylin, JHU**

**“Bringing Epigenetic Therapy to the Management of Ovarian and Other Cancers”**

**Goal: Determine the role of epigenetic drugs in combination with DNA repair inhibitors in ovarian cancer. My current role is bench mentorship/support of graduate student undertaking qRT-PCR expression analysis and functional DNA repair capacity assays.**

**Role: Other personnel**

**Effort: 0%**

**Van Andel Research Institute PI: F. Rassool**

**“Use of DNA Demethylating Agents and PARP Inhibitors in Enhancing Immune Responses in Cancer”**

**Goal:** Correlative studies to support phase 2 clinical trial testing decitabine/talazoparib drug combination in AML. I have led development of *in vitro* DNA repair capacity assays and proximity ligation protein interaction assays for use by lab members, and performed qRT-PCR gene expression analysis**.**

**Role: Other personnel**

**Effort: 0%**

**NIEHS (2R01ES011858) MPI: S. Baylin, F. Rassool, S. Easwaran**

**“DNA Methyltransferase Gene Expression in Colon Cancer”**

**Goal: To** study the role of PARP1 and DNMT1 in DNA repair and aging in the context of colon cancer**. My current focus is to undertake experiments in colon cancer organoids to determine function and dynamics of methylation complex following DNA damage, including immunostaining for protein accumulation at irradiation damage sites, protein-protein interactions via proximity ligation immunofluorescence assay.**

**Role: Other personnel**

**Effort: 0%**

**Leukemia & Lymphoma Society PI: F. Rassool**

**“DNA Demethylating Agent and PARP Inhibitor Therapy Targeting Aberrant DNA Repair in Acute Myeloid Leukemia”**

Goal: Study sensitization of leukemias to PARP inhibitors via low-dose epigenetic therapy in AML stem cells. My main role is bench supervision and assistance to a graduate student who is performing gene expression analysis and functional assays of DNA repair and cytotoxicity in AML cells.

**Role: Other personnel**

Effort: 0%