BIOGRAPHICAL SKETCH

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NAME: Richardson, Paul G

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

POSITION TITLE: Professor of Medicine

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 Date MM/YYYY	FIELD OF STUDY
Medical College of St. Bartholomew's Hospital, University of London, London, United Kingdom	MBBS	1986	Medicine

Personal Statement

After certification in Internal Medicine, Hematology and Medical Oncology, as well as working in Cancer Pharmacology from 1994 onwards at Dana-Farber Cancer Institute (DFCI), I joined the Jerome Lipper Myeloma Center in 1999, was appointed Clinical Director in 2001, and led the development of several novel drugs including bortezomib, lenalidomide and pomalidomide. Subsequent studies have focused on next generation novel drugs including histone deacetylase inhibitors such as panobinostat and other small molecules including the second generation proteasome inhibitors NPI 0052 (also known as marizomib) and MLN 9708 (also known as ixazomib) with the goal of further improving patient outcome. More recently, my clinical innovations have been in the development of the breakthrough monoclonal antibodies elotuzumab and daratumumab for the treatment of both untreated and relapsed myeloma. Previously, my senior investigator role in the VISTA trial comparing bortezomib in combination with melphalan and prednisone versus melphalan and prednisone alone as part of an international Phase 3 trial established bortezomib, melphalan and prednisone (VMP) as a new treatment standard in patients not eligible for stem cell transplant. At present, my major effort is focused on the Intergroup Francophone Myelome (IFM)/DFCI clinical trial in newly diagnosed patients eligible for stem cell transplant treated with lenalidomide, bortezomib and dexamethasone (so-called RVD). This regimen has generated an unprecedented response rate, leading to its adoption in this international study, which incorporates genomic and proteomic evaluation to establish a future platform for tailored therapy. Other important contributions include the management of treatment-emergent neuropathy in myeloma. Similarly, the development of defibrotide for the treatment and prevention of hepatic veno-occlusive disease following stem cell transplantation has been aimed at improving therapeutic outcome, with defibrotide emerging as the most promising agent for this unmet medical need. I have published extensively, having authored or co-authored over 280 original articles and 190 reviews, chapters, and editorials in peer-reviewed journals. In addition to holding positions on the Editorial Boards of leading journals, I am prior Chairman of the Multiple Myeloma Research Consortium (MMRC), Clinical Trials Core, a position held for 5 years as part of a rotating tenure, and for which I continue on the Steering and Project Review Committee. I was also a member of ASCO Hematologic Malignancies Subcommittee for the required one year term. More recently, I was appointed Chair of the Alliance Myeloma Committee. Honors include the George Canellos Award for Excellence in Clinical Research and Patient Care, and The Tisch Outstanding Achievement Award for Clinical Research, as well an honorary Fellowship of the Royal College of Physicians (UK), given in recognition for international contributions in multiple myeloma and stem cell transplantation. I was a co-recipient of the Warren Alpert Foundation Prize in recognition of the successful therapeutic targeting of the ubiquitin-proteasome pathway. I was also a co-recipient of the Accelerator Award for contributions to clinical research and patient enrollment in MMRC studies, as well as for the Research Center of the Year Award in 2009. I was ranked by Thomson Reuters Science Watch amongst the top 19 investigators at DFCI for the most highly cited research. Most recently, I was a co-recipient of the ASH Ernest Beutler Prize for clinical science and translational research in the development of proteasome inhibition as an effective treatment strategy for multiple myeloma.

1. **Richardson PG**, Sonneveld P, Schuster MW, et al. Assessment of Proteasome Inhibition for Extending Remissions (APEX) Investigators. Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. *N Engl J Med*. 2005 Jun 16;352(24):2487-98. PMID: 15958804
2. San Miguel JF, Schlag R, Khuageva NK, Dimopoulos MA, Shpilberg O, Kropff M, Spicka I, Petrucci MT, Palumbo A, Samoilova OS, Dmoszynska A, Abdulkadyrov KM, Schots R, Jiang B, Mateos MV, Anderson KC, Esseltine DL, Liu K, Cakana A, van de Velde H, **Richardson PG;** VISTA Trial Investigators. Bortezomib plus melphalan and prednisone for initial treatment of multiple myeloma. *N Engl J Med.* 2008 Aug 28;359(9):906-17. PMID: 18753647
3. **Richardson PG**, Weller E, Lonial S, et al. Lenalidomide, bortezomib, and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma. *Blood*. 2010 Aug 5;116(5):679-86. PMID: 20385792
4. **Richardson PG**, Siegel DS, Vij R, et al. Pomalidomide alone or in combination with low-dose dexamethasone in relapsed and refractory multiple myeloma: a randomized phase 2 study. *Blood*. 2014 Mar 20;123(12):1826-32. PMID: 24421329

B. Positions and Honors

Positions and Employment

1986 – 1987	[Intern] Pre-registration House Surgeon and Physician, Departments of Medicine & Surgery, St. Bartholomew's Hospital, University of London, UK
1987 – 1990	[Senior Resident] Senior House Officer, Department of Medicine, Newcastle University School of Medicine Newcastle General and Freeman Hospitals, Newcastle-upon-Tyne, UK
1990 – 1991	[Chief Resident] Senior House Officer, Department of Medicine Royal Marsden Hospital, London and Surrey, UK
1995 – 1997	[Resident] Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA
1991 – 1994	Clinical Fellow, Division of Hematology and Oncology, Department of Medicine, Tufts University School of Medicine, Baystate Medical Center, Springfield, MA
1993 – 1994	Visiting Fellow, Division of Medical Oncology, Department of Medicine, DFCI, Boston, MA
1994 – 2003	Instructor of Medicine, Harvard Medical School, DFCI, Boston, MA
2001 – 2014	Clinical Director, Jerome Lipper Multiple Myeloma Center, DFCI, Boston, MA
2003 – 2006	Assistant Professor of Medicine, Harvard Medical School, DFCI, Boston, MA
2006 -	Associate Professor of Medicine, Harvard Medical School, DFCI, Boston MA
2012-	RJ Corman Professor of Medicine, Harvard Medical School, DFCI, Boston, MA
2014 -	Clinical Program Leader, Director of Clinical Research, Jerome Lipper Multiple Myeloma Center, DFCI, Boston, MA

Other Experience and Professional Memberships

1995	American Society of Clinical Oncology, Member
1997	American Society of Hematology, Member
1999	American College of Physicians
2001-2009	Institutional Review Board, Member, DFCI
2004-2009	Multiple Myeloma Research Consortium (MMRC), Chairman, Clinical CORE
2005	American Society of Clinical Oncology (ASCO) Research Committee
2006	American Society of Hematology/Food and Drug Administration, Multiple Myeloma (MM) Committee Member and Sub-Committee Chairman, Special Task Force for Impending Drug Approval
2006	VOD/SOSS Subcommittee, Member, State of the Science Symposium, Blood and Bone Marrow Transplant, Clinical Trials Network (NHLBI/NCI)
2007-2009	Chairman, Data Management and Safety Board (DMSB), Pediatric Study of Defibrotide as Prophylaxis against VOD in Stem Cell Transplant Recipients; a Randomized, Controlled Trial, European Group for Blood and Marrow Transplantation (EBMT)
2008-2014	Co-Chairman, Independent Review Committee (IRC), Carfilzomib studies in relapsed MM
2011-	Chairman, Myeloma Committee, Alliance for Clinical Trials in Oncology
2012-	Scientific Steering Committee Member, NCI Multiple Myeloma Committee
2013-	Committee Member, Executive Committee for Clinical Research, DFCI
2014-	Member, Multiple Myeloma Sub-Committee, Clinical Trials Network (CTN), ASBMT

Honors

1995 Emil Frei III Fellowship Award
1997 Lee Beckenstein Fellowship Award
2002 The Society of Teaching Scholars, Brigham and Women's Hospital
2004 George Canellos Award for Excellence in Clinical Research and Patient Care, DFCI
2004 Partners in Excellence Award, DFCI
2006 Partners in Excellence Award, DFCI
2008 Tisch Family Outstanding Achievement Award in Translational Research
2008 Schwartz Cancer Center Compassionate Caregiver Award
2009 Fellowship of the Royal College Of Physicians (FRCP), London, UK
2012 Warren Alpert Foundation Prize, Harvard Medical School
2015 Ernest Beutler Lecture and Prize, American Society of Hematology

C. Contribution to Science

1. *New drug development in multiple myeloma*. Novel agents in the treatment of multiple myeloma have resulted in significant improvements in overall survival and patient outcome. My contributions in this area have included the development of bortezomib, and then lenalidomide as a key immunomodulatory agent in the treatment of the disease, as well as the subsequent development of pomalidomide as a next-generation immunomodulatory drug after lenalidomide failure. Further, the development of ixazomib as the first oral boronate peptide has been an important contribution in this setting.
    a. **Richardson PG**, Barlogie B, Berenson J, et al. A phase 2 study of bortezomib in relapsed, refractory myeloma. *N Engl J Med.* 2003 Jun 26;348(26):2609-17. PMID: 12826635
    b. **Richardson PG**, Schlossman RL, Weller E, et al. Immunomodulatory drug CC-5013 overcomes drug resistance and is well tolerated in patients with relapsed multiple myeloma. *Blood*. 2002 Nov 1;100(9):3063-7. PMID: 12384400
    c. **Richardson PG**, Siegel D, Baz R, et al. Phase 1 study of pomalidomide MTD, safety, and efficacy in patients with refractory multiple myeloma who have received lenalidomide and bortezomib. *Blood*. 2013 Mar 14;121(11):1961-7. PMID: 23243282
    d. **Richardson PG**, Baz R, Wang M, et al. Phase 1 study of twice-weekly ixazomib, an oral proteasome inhibitor, in relapsed/refractory multiple myeloma patients. *Blood*. 2014 Aug 14;124(7):1038-46. PMID: 24920586
2. *Novel combinations in multiple myeloma.* In the context of novel treatments for multiple myeloma improving outcome, combinatorial strategies have been critical. These have typically been informed by laboratory studies. Examples include the combination of lenalidomide and bortezomib, and the exploration of AKT inhibition with both immunomodulatory drugs and proteasome inhibitors. Additional studies have included histone deacetylase inhibitors in combination with other backbone agents. Finally, the development of ixazomib and its combination with lenalidomide and dexamethasone has resulted in a highly effective regimen in the upfront setting and also has been extensively tested in the relapsed and refractory setting as part of the TOURMALINE program.
    a. **Richardson PG**, Weller E, Jagannath S, et al. Multicenter, Phase I, Dose-Escalation Trial of Lenalidomide Plus Bortezomib for Relapsed and Relapsed/Refractory Multiple Myeloma. *J Clin Oncol*. 2009 Dec 1;27(34):5713-9. PMID: 19786667
    b. **Richardson PG**, Wolf J, Jakubowiak A, et al. Perifosine plus bortezomib and dexamethasone in patients with relapsed/refractory multiple myeloma previously treated with bortezomib: results of a multicenter phase I/II trial. *J Clin Oncol*. 2011 Nov 10;29(32):4243-9. PMID: 21990396
    c. **Richardson PG,** Schlossman RL, Alsina M, et al. PANORAMA 2: panobinostat in combination with bortezomib and dexamethasone in patients with relapsed and bortezomib-refractory myeloma. *Blood*. 2013 Oct 3;122(14):2331-7. PMID: 23950178
    d. Kumar SK, Berdeja JG, Niesvizky R, Lonial S, Laubach JP, Hamadani M, Stewart AK, Hari P, Roy V, Vescio R, Kaufman JL, Berg D, Liao E, Di Bacco A, Estevam J, Gupta N, Hui AM, Rajkumar V, **Richardson PG**. Safety and tolerability of ixazomib, an oral proteasome inhibitor, in combination with lenalidomide and dexamethasone in patients with previously untreated multiple myeloma: an open-label phase 1/2 study. *Lancet Oncol*. 2014 Dec;15(13):1503-12. PMID: 25456369
3. *Immuno-therapeutics in multiple myeloma.* A key barrier to success in the treatment of multiple myeloma has been immune-paresis. Moreover, the integration of monoclonal antibody therapy has

been a key area of progress in developmental therapeutics. In this regard, I have provided leadership in the development of elotuzumab as well as daratumumab as a breakthrough treatment.

a. Lonial S, Dimopoulos M, Palumbo A, White D, Grosicki S, Spicka I, Walter-Croneck A, Moreau P, Mateos MV, Magen H, Belch A, Reece D, Beksac M, Spencer A, Oakervee H, Orlowski RZ, Taniwaki M, Röllig C, Einsele H, Wu KL, Singhal A, San-Miguel J, Matsumoto M, Katz J, Bleickardt E, Poulart V, Anderson KC, **Richardson P**; ELOQUENT-2 Investigators. Elotuzumab Therapy for Relapsed or Refractory Multiple Myeloma. *N Engl J Med.* 2015 Aug 13;373(7):621-31. PMID: 26035255
b. Lokhorst HM, Plesner T, Laubach JP, Nahi H, Gimsing P, Hansson M, Minnema MC, Lassen U, Krejcik J, Palumbo A, van de Donk NW, Ahmadi T, Khan I, Uhlar CM, Wang J, Sasser AK, Losic N, Lisby S, Basse L, Brun N, **Richardson PG**. Targeting CD38 with Daratumumab Monotherapy in Multiple Myeloma. *N Engl J Med.* 2015 Sep 24;373(13):1207-19. PMID: 26308596
c. **Richardson PG,** Jagannath S, Moreau P, et al. Elotuzumab in combination with lenalidomide and dexamethasone in patients with relapsed multiple myeloma: final phase 2 results from the randomised, open-label, phase 1b-2 dose-escalation study. *Lancet Haematol.* 2015 Dec;2(12):e516-27. PMID: 26686406
d. Plesner T, Arkenau HT, Lokhorst HM, Gimsing P, Krejcik J, Lemech C, Minnema MC, Lassen U, Laubach JP, Ahmadi T, Yeh H, Guckert ME, Feng H, Brun NC, Lisby S, Basse L, Palumbo A, and **Richardson PG**. Safety and Efficacy of Daratumumab with Lenalidomide and Dexamethasone in Relapsed or Relapsed, Refractory Multiple Myeloma. Proceedings of the American Society of Hematology meeting; Dec 6-9; San Francisco, CA. *Blood*, 2014; 124(21): [abstract 84].

4. *Integration of stem cell transplantation in the management of younger patients with multiple myeloma.* With the advent of the novel agents as well as monoclonal antibodies, the position of autologous stem cell transplantation in the management of younger multiple myeloma patients has become a critical question. The pivotal IFM/DFCI 2009 study examining the role of early versus late transplant with a comprehensive examination of both patient and disease characteristics is the current leading trial examining the question.The development of effective upfront induction strategies as well as the integration of maintenance and consolidation has been a vital part of this. Moreover, the development of other combinations (including all oral approaches) provide important forward directions in the future.
    a. **Richardson PG**, Weller E, Lonial S, et al. Lenalidomide, bortezomib, and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma. *Blood*. 2010 Aug 5;116(5):679-86. PMID: 20385792
    b. Kumar S, Flinn I, **Richardson PG,** et al. Randomized, multicenter, phase 2 study (EVOLUTION) of combinations of bortezomib, dexamethasone, cyclophosphamide, and lenalidomide in previously untreated multiple myeloma. *Blood.* 2012 May 10;119(19):4375-82. PMID: 22422823
    c. McCarthy PL, Owzar K, Hofmeister CC, Hurd DD, Hassoun H, **Richardson PG,** Giralt S, Stadtmauer EA, Weisdorf DJ, Vij R, Moreb JS, Callander NS, Van Besien K, Gentile T, Isola L, Maziarz RT, Gabriel DA, Bashey A, Landau H, Martin T, Qazilbash MH, Levitan D, McClune B, Schlossman R, Hars V, Postiglione J, Jiang C, Bennett E, Barry S, Bressler L, Kelly M, Seiler M, Rosenbaum C, Hari P, Pasquini MC, Horowitz MM, Shea TC, Devine SM, Anderson KC, Linker C. Lenalidomide after stem-cell transplantation for multiple myeloma. *N Engl J Med.* 2012 May 10;366(19):1770-81. PMID: 22571201
    d. **Richardson PG,** Hofmeister CC, Rosenbaum CA, et al. Twice-Weekly Oral MLN9708 (Ixazomib Citrate), An Investigational Proteasome Inhibitor, In Combination With Lenalidomide (Len) and Dexamethasone (Dex) In Patients (Pts) With Newly Diagnosed Multiple Myeloma (MM): Final Phase 1 Results and Phase 2 Data. Proceedings of the American Society of Hematology meeting; Dec 7-10; New Orleans, LA. *Blood*, 2013; 122(21):535. [abstract 535]

5. *Management of toxicities in multiple myeloma and other settings.* Critical to improving outcome in patients with multiple myeloma has been improving the tolerability of therapy. This is particularly true in the management of peripheral neuropathy in which I have led comprehensive efforts to examine the neurotoxicity of bortezomib prospectively and generate effective treatment strategies. In the context of autologous stem cell transplantation and allogeneic transplant, one of the barriers to cure has been fatal regimen-related toxicities associated with conditioning and endothelial damage. My research efforts in this area have resulted in the development of defibrotide for the treatment of veno-occlusive

disease and sinusoidal obstruction syndrome with this agent. This agent may also prove effective in other microangiopathies associated with transplant. Moreover, there may also be an emerging role for this drug to abrogate the vascular complications associated with graft versus host disease.

a. **Richardson PG,** Xie W, Mitsiades C, et al. Single-agent bortezomib in previously untreated multiple myeloma: efficacy, characterization of peripheral neuropathy, and molecular correlations with response and neuropathy. *J Clin Oncol.* 2009 Jul 20;27(21):3518-25. PMID: 19528374
b. **Richardson PG**, Delforge M, Beksac M, et al. Management of treatment-emergent peripheral neuropathy in multiple myeloma. *Leukemia*. 2012 Apr;26(4):595-608. PMID:22193964
c. **Richardson PG**, Murakami C, Jin Z, et al. Multi-institutional use of defibrotide in 88 patients after stem cell transplantation with severe veno-occlusive disease and multisystem organ failure: response without significant toxicity in a high-risk population and factors predictive of outcome. *Blood*. 2002 Dec 15;100(13):4337-43. PMID: 12393437
d. **Richardson PG**, Soiffer RJ, Antin JH, et al. Defibrotide for the treatment of severe hepatic veno-occlusive disease and multi-organ failure post stem cell transplantation: a multi-center, randomized, dose-finding trial. *Biol Blood Marrow Transplant*. 2010 Jul;16(7):1005-17. PMID: 20167278

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/44031993/?sort=date&direction=descending

D. Research Support

Active

P01CA78378 (Anderson) 08/01/1998 – 03/31/2016 (NCE)
NIH/NCI – Project 1
Host-Tumor Cell Interactions in Myeloma: Therapeutic Applications
Targeting Myeloma Cell-Host Bone Marrow Interactions
The major goals of this project are to enhance our understanding of the intercellular interaction of MM cells with pDCs and its therapeutic relevance, and specifically addresses three inter-related hypotheses: 1) the biological behavior of MM cells is modulated by their interactions with pDCs; 2) the molecular and functional sequelae of pDC-MM interactions represent potential therapeutic targets; and 3) the aggregate interplay of these interactions in vivo allows for the rational design of novel single and combination targeted therapies.
Role: Investigator

P01CA1555258 (Munshi) 09/01/2011-08/31/2016
NIH/NCI – Project 1
Integrative Oncogenomics in Multiple Myeloma
Role of Combination Therapy with Novel Targeted Agents and High-Dose Therapy in Newly-Diagnosed Myeloma
The major goal of this project is to determine role of high-dose therapy in the era of novel agent therapy and will allow development of definition of stringent Cr for clinical application.
Role: Investigator

P50CA100707 (Anderson) 09/01/2014 – 08/31/2018
NIH/NCI
Specialized Program of Research Excellence
Targeting Deubiquitylating Enzymes in Multiple Myeloma (Project 1)
This new paradigm to target UPS pathways in MM, either at the level of proteasome or deubiquitylating enzymes, has great promise not only to change the natural history of MM, but also to serve as a model for targeted therapeutics in other cancers.
Role: Investigator

Completed

None