

Name: Roxana Octavia Carare MD PhD

Present Appointment: Professor of Clinical Neuroanatomy

Dates	Appointment
Aug 2016- present	Professor of Clinical Neuroanatomy
Aug 2014-July 2016	Associate Professor Clinical Neuroanatomy
Mar 2013-July 2014	Senior Lecturer Clinical Neurosciences, University of Southampton
Apr 2001-Feb 2013	Lecturer Anatomical Sciences, University of Southampton
Sept 1998-Apr 2001	Teaching Assistant, Anatomical Sciences, University of Southampton
1st April 1997 – 1st July 1997	Clinical Attachments: Accident & Emergency, Care of the Elderly, Internal Medicine – Stoke Mandeville Hospital, Aylesbury, Bucks
1st Aug 1996-1st Jan 1997	Clinical Attachment: General Surgery- St Columcille's Hospital, Dublin
1st Feb 1996-31st July 1996	Senior resident in General Surgery- Colentina Hospital, Bucharest, Romania
1st Nov 1995-31st Jan 1996	Resident in Paediatrics- Fundeni Hospital, Bucharest, Romania
1st May 1995-30th Oct 1995	Resident in General Medicine- Colentina Hospital, Bucharest, Romania
1st Feb 1995-30th April 1995	Resident in General Surgery- Colentina Hospital, Bucharest, Romania

Date	Title of Award	Subject	Awarding Body
July 1994	Doctor of Medicine	General Medicine	University of Medicine and Pharmacy "Carol Davila" Bucharest, Romania
January 2006	PhD	Neuropathology	University of Southampton

Publications H index 40 <https://pubmed.ncbi.nlm.nih.gov/?term=Carare+R&sort=date>

1. O'Sullivan E, *Carare-Nnadi RO*, Greenslade J, Bowyer G. Clinical significance of variations in the interconnections between flexor digitorum longus and flexor hallucis longus in the region of the knot of Henry. *Clinical Anatomy* 2005 Mar;18(2):121-5
2. Schley D, *Carare-Nnadi RO*, Please CP, Perry VH, Weller RO. Mechanisms to explain the reverse perivascular transport of solutes out of the brain. *Journal of Theoretical Biology*, 2006, 238:962-974
3. Campbell S; *Carare-Nnadi RO*; Losey P.H; Anthony D. Loss of the atypical inflammatory response in juvenile and aged rats. *Neuropathology and Applied Neurobiology* 2007, 33, 108-120
4. *Carare RO*, Bernardes-Silva M, Newman TA, Page AM, Nicoll JAR, Perry VH, Weller RO. Solute, but not cells, drain from the brain parenchyma along basement membranes of capillaries and arteries. Significance for cerebral amyloid angiopathy and neuroimmunology. *Neuropathology and Applied Neurobiology* 2008 Apr;34(2):131-44. *The most cited article in Neuropathology and Neurobiology in 2010. Cited by 171 in Jan 2016.*
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6. De Silva P, *Carare RO*, Weller R.O. Failure of elimination of Amyloid-beta from the brain in Alzheimer's Disease. Opportunities for prevention and therapy. *Progress in Neurology and Psychiatry*, 2008 May; 12(4):6-10
7. Weller RO, Subash M, Preston SD, Mazanti I, *Carare RO*. Perivascular drainage of amyloid beta peptides from the brain and its failure in cerebral amyloid angiopathy and Alzheimer's disease. *Brain Pathol.* 2008 Apr;18(2):253-66.
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10. Clapham R, O'Sullivan E, Weller RO, *Carare RO*. Cervical lymph nodes are found in direct relationship with the carotid arteries. *Clinical Anatomy* 2010 Jan;23(1):43-7.

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 12. Jowett A, Sheikh F, Carare RO., Goodwin M. Posterolateral approach to the posterior malleolar fracture and the location of the sural nerve. *Foot and Ankle International* 2010 Oct;31(10):880-3
 13. Coleman, P.G., Carare RO, Petrov, I., Forbes, E., Saigal, A., Spreadbury, J., Yap, A. & Kendrick, T. Spiritual belief, social support, physical functioning and depression among older people in rural areas in Bulgaria and Romania. *Ageing and Mental Health*, 2011, Apr 15(3), 327-333
 14. Hawkes CA, Härtig W, Kacza J, Schliebs R, Weller R.O, Nicoll JAR, Carare RO Perivascular drainage of solutes is impaired in the ageing mouse brain and in the presence of cerebral amyloid angiopathy. *Acta Neuropathologica*, 2011, Apr 121(4), 431-443.
 15. Carare RO and Hawkes CA. Alzheimer's disease: A Failure of Clearance of soluble metabolites from the ageing brain. Editorial. *Addiction Research and Therapy*, 2011, S5
 16. Teeling J, Carare RO (joint first authors), Glennie M.J, Perry VH. The formation of immune complexes in the brain induces inflammation that depends on Fc Receptor interaction. *Acta Neuropathol*. 2012 Oct;124(4):479-90.
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 19. Hawkes, CA, Shaw J.E, Brown M, Sampson A.P, McLaurin J, Carare RO. MK886 reduces cerebral amyloid angiopathy severity in the TgCRND8 mouse model of AD. *Neurodegenerative Diseases*, 2013 13(1):17-23
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 24. Bueche C, Hawkes CA, Garz C, Vielhaber S, Attems A, Knight RT, Heinze H, Carare RO, Schreiber S Hypertension drives β -amyloid accumulation in the brain parenchyma. *Ann Clin Transl Neurol*. 2014 Feb;1(2):124-9.
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39. Osman S, Carare RO. Barriers faced by the people with dementia in the black and minority ethnic groups in accessing health care and social services. *Journal of Gerontology and Geriatrics Research*
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41. Zekonyte J, Sakai K, Nicoll J, Weller RO, Carare RO. Quantification of molecular interactions between apoE, Amyloid-beta (A β) and laminin: Relevance to accumulation of A β in Alzheimer's disease. *Biophysica et Biochimica Acta, Molecular Basis of Disease* 2015
42. UK Biobank Eyes & Vision Consortium. Frequency and Distribution of Refractive Error in Adult Life: Methodology and Findings of the UK Biobank Study *PLoS One* 2015 Oct 2;10(10) 2016-2017
43. Diem AK, Tan M, Bressloff NW, Hawkes CA, Morris AWJ, Weller RO, Carare RO. A Simulation Model of Periarterial Clearance of Amyloid-beta from the Brain; *Frontiers in Aging Neuroscience* 2016 Feb 12;8:18.
44. Manousopoulou A..Carare RO*, Garbis SD**joint senior authors* Hemisphere asymmetry of pharmacologic response to treatment in an Alzheimer's disease mouse model. *Journal of Alzheimer's disease*, 2016;51(2):333-8.
45. Coloma M, Schaffer D, Carare RO, Chiarot P, Pulsations with Reflected Boundary Waves: A Hydrodynamic Reverse Transport Mechanism for Perivascular Drainage in the Brain. *Journal of Mathematical Biology* 2016 Aug;73(2):469-90. doi: 10.1007/s00285-015-0960-6.
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47. Bakker E, Bacskai BJ, Aldea R, Arbel-Ornath M, Bedussi B, Weller RO Lymphatic drainage of the brain: perivascular, paravascular and significance for neurodegenerative diseases. *Carare RO. Cellular and Molecular Neurobiology*, 2016 Mar 18.
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50. Engelhardt B, Carare RO, Bechmann I, Flügel A, Laman JD, Weller RO. Vascular, glial and lymphatic immune gateways of the central nervous system. *Acta Neuropathologica*, 2016 Sep;132(3):317-38.
51. Manousopoulou A, Gatherer M, Smith C, Nicoll JA, Woelk CH, Johnson M, Kalaria R, Attems J, Garbis SD, Carare RO. Systems proteomic analysis reveals that Clusterin and Tissue Inhibitor of Metalloproteinases 3 increase in leptomeningeal arteries affected by CAA. *Neuropathol Appl Neurobiol.* 2016 Oct;43(6):492-504.

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68. Aldea R...*Carare RO*, Richardson G. Cerebrovascular smooth muscle cells as the drivers of IPAD. *Frontiers in Aging Neuroscience*, Jan 2019.
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76. Schreiber S, ...Carare RO, Werring DJ. Invited Review: The spectrum of age-related small vessel diseases. *Neuropathol Appl Neurobiol* 2019 Aug 6.
77. Khawaja AP, Chua S...Biobank Eye and Vision Consortium. Comparison of Associations of different macular inner retinal thickness parameters in a large cohort: the UK Biobank. *Ophthalmology*, 2019
78. Mazur C, ...Carare RO, Verma A. Brain pharmacology of intrathecal antisense oligonucleotides revealed through multimodal imaging . *JCI Insight*, Oct 17;4(20), 2019
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87. Gafson AR...Carare RO...Matthews PM. Neurofilaments: neurobiological foundations for biomarker applications. *Brain* 2020 May14
88. Khawaja A.P....Carare RO...UK Biobank Eye and Vision Consortium. Comparison of Associations with different macular inner retinal thickness parameters in a large cohort: the UK biobank. *Ophthalmology* 2020. Jan;127(1):62-71
89. Keable AC...Carare RO. ApoE4 astrocytes secrete basement membranes rich in fibronectin and poor in laminin compared to ApoE3 astrocytes. *In Press*, *International Journal of Molecular Sciences*. IF 4.18
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91. Nimmo J,...Carare RO. Peri-Arterial Pathways for clearance of α -Synuclein and tau from the brain: Implications for the pathogenesis of dementias and for immunotherapy. *Alzheimer's & Dementia: Alzheimers Dement (Amst)*. 2020 Jul 28;12(1)
92. Carare RO... Verma A. Clearance of interstitial fluid (ISF) and CSF (CLIC) group—part of Vascular Professional Interest Area (PIA) Cerebrovascular disease and the failure of elimination of Amyloid- β from the brain and retina with age and Alzheimer's disease-Opportunities for Therapy. *Alzheimer's & Dementia(Amst)*. Aug 3;12(1)
93. Macgregor-Sharp MT.... Carare RO. Demonstrating a reduced capacity for removal of fluid from cerebral white matter and hypoxia in areas of White Matter Hyperintensity associated with age and dementia. *Acta Neuropathologica Communications*, 2020 Aug 8;8(1):131.
94. Hosoki S...Carare RO...Ihara M. Oral carriage of *Streptococcus mutans* harboring the *cnm* gene relates to an increased incidence of cerebral microbleeds. *Stroke*. 2020;51:00–00.
95. Saito S...Carare RO...Ihara M. Cerebral amyloid angiopathy presenting as massive subarachnoid haemorrhage: a case study and review of literature. *Frontiers In Aging Neuroscience* 2020, 10;12:538456.
96. Manousopoulou A... Carare RO. Quantitative proteomic profiling of white matter in cases of cerebral amyloid angiopathy reveals upregulation of extracellular matrix proteins and clusterin. *In Press*, *Free Neuropathology*.
97. Saito S, McLaurin J, Carare RO. Editorial: Intramural vascular cells: key therapeutic targets for VCI. *Front Aging Neurosci.* 2020 Oct 30;12:615780.

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100. Nizari S, Wells JA, Carare RO, Romero IA, Hawkes CA. Loss of cholinergic innervation differentially affects e-nos mediated blood flow, drainage of Abeta and CAA. *Acta Neuropathol Commun*. 2021 Jan 7;9(1):12.
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105. UK Biobank Eye and Vision Consortium. Genome wide meta-analysis identifies 127 open angle glaucoma loci with consistent effect across ancestries. *Nat Commun*. 2021 Feb 24;12(1):1258.
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109. Varatharaj A, Carare RO, Weller RO, Gawne-Cain M, Galea I. Drainage of interstitial solutes from brainstem visualised along cranial nerves in man. *Proc Natl Acad Sci U S A*. 2021 Nov 9;118(45):e2106331118. doi: 10.1073/pnas.2106331118.
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113. Li M,Carare RO..Horsburgh K. Impaired Glymphatic Function and Pulsation Alterations in a Mouse Model of Vascular Cognitive Impairment. *Front. Aging Neurosci*. 13:788519.doi: 10.3389/fnagi.2021.788519

Book Chapters

1. Weller RO, Carare RO; Boche D. Ageing and the accumulation of amyloid in brain parenchyma and blood vessel walls in Alzheimer's disease. *Encyclopedia of Neuroscience* 2009, Vol 1; pp 355-362. (L.R. Squire, Editor). Oxford: Academic Press.
2. Weller RO, Carare RO, Hawkes CA, Galea I. Chapter 19 – Pathophysiology of Lymphatic Drainage of the Central Nervous System. In *Multiple Sclerosis, A mechanistic view*. Elsevier, 2016. ISBN: 978-0-12-800763-1
3. Sharp MM, Page A, Morris A, Weller RO, Carare RO. Quantitative assessment of cerebral basement membranes using electron microscopy. *Methods Mol Biol*. 2017;1559:367-375.
4. Albargothy NJ, Sharp MM, Gatherer M, Morris A, Weller RO, Hawkes C, Carare RO. Investigating the Lymphatic Drainage of the Brain. *Essential Skills and Tools. Methods Mol Biol*. 2017;1559:343-365.

Grants:

- Sept 2012-Sept 2017: Alzheimer's Research UK: Interaction of systemic and central apolipoproteins in the pathogenesis and treatment of cerebral amyloid angiopathy, £264,589
- Sept 2014-Aug 2017: Biogen Ltd. Defining the connections between the subarachnoid space and the brain parenchyma. £75,000
- Aug 2014: Equipment grant: SP8 Confocal. Alzheimer's Research UK, £100,000
- October 2014-January 2016: Invicro Ltd. Study of the pattern of intracerebral distribution of small molecules £66,870
- Feb 2015: Co-applicant for equipment grant (Nano-Zoomer XR). Alzheimer's Research UK, £100,000
- October 2015-Sept 2019: ARUK: Co-PI Targeting perivascular innervation and vascular tone for improved clearance of β -amyloid from the brain. £88,440
- October 2015-Sept 2019: BBSRC CASE Studentship: Developing a new in vitro model for the study of perivascular clearance. £95,042
- March 2017-Feb 2018: Rosetrees Trust. Does maternal high fat diet lead to dementia? £25,000
- Sept 2013-Sept 2017. BBSRC: Physiology of perivascular drainage of the brain and how it is affected by advancing age. £600,000
- Aug 2016-Sept 2017: British Neuropathological Society. Aquaporin in white matter abnormalities £15,000
- Mar 2018-Feb 2020: United Neuroscience. New immunization strategies for Alzheimer's disease. £250,000
- Sept 2017-Dec 2020: Stroke Association. Vascular dementia: failure of fluid drainage from cerebral white matter. £200,131.
- Sept 2017-Aug 2020: National Institute of Health, award to Binghamton, Cornell and Southampton Universities. Interdisciplinary assessment of IPAD, £51,700 (Southampton component)
- Oct 2017-Sept 2020: Medical Research Council UK & United Neurosciences: Immunization in alpha synucleinopathies. £70,000
- Aug 2020-July 2021 Alzheimer's Research UK: Adrenergic and cholinergic receptors of the blood vessels as key players in Alzheimer's disease. £99,924

Current active grants

- Apr 2020-Oct 2021: United Neuroscience. New immunization strategies for Alzheimer's disease. £167,799
- Apr 2019-Mar 2022: Japan Society of Science fellowship to Dr Satoshi Saito. The role of clusterin in facilitating IPAD. £164,000
- May 2019-Apr 2023: Horizon 2020 TUBE-LC-MG-2018 £239,039
- Oct 2019-Oct 2021 Royal Society: Lysyl Oxidase (LOX) as facilitator of intramural periaarterial drainage of the brain £24,000
- Sept 2020-Aug 2023. Bright Focus (USA- award with Michigan State University) Noradrenergic regulation of amyloid clearance in AD. Total \$285,000 . Southampton award: £109,647
- Aug 2020-July 2023 Alzheimer's Association (USA): Targeting cerebral smooth muscle cell mitochondria in Alzheimer's disease \$44,583
- Jan 2021-Dec 2022 CODIAK Biosciences, Exosomes in Neurological diseases £373,727
- May 2021-Apr 2023 VAXXINITY, "Effects of anti-tau immunization" £185,000
- May 2021-Apr 2023 ALCYONE, "Patterns of distribution of AAV9" £142,335
- May 2021-Apr 2022 Private Donation £50,000 from USA
- Aug 2021-July 2022 YUMANITY "Targeting Stearoyl-CoA-Desaturase (SCD) in the Brain" £211,522
- Jan 2022-July 2022 ALNYLAM "Biodistribution of RNAi Agents in Mouse brain by Confocal Imaging Analysis", £59,666
- Mar 2022-Feb 2024 NIH "Perlecan Domain V as a therapeutic VCID strategy for the clearance of amyloid beta from the brain in cerebral amyloid angiopathy", £ 76,645
- Jul 2021-Jul 2023: PCE Romania- Clusterin as a therapeutic agent in Alzheimer's disease 249,635 EUR

Roles and activities

Fellow of the Higher Education Academy. Chair of the Equality, Diversity and Inclusivity Committee Faculty of Medicine, University of Southampton, Visiting Knowledge Exchange Fellow, University of Winchester, Home Office Licensed Teacher of Anatomy. Honorary Consul for Romania. Member of: PRIME- International Medical Education, British Pathological Society, Association for the Study of Medical Education, British Neuroscience Association, British Neuropathological Society, Federation of European Neuroscience Societies, International Brain Research Organisation, British Association of Clinical Anatomists, Anatomical Society, International Alzheimer's Disease Forum, Association for the Study of Medical Education. Member of the Scientific Committee for Cerebral Amyloid Angiopathy 2014. Member of Scientific Committee for Vas-Cog 2015, 2020. Invited member of Cerebral Autoregulation Research Network. Associate Editor Frontiers in Aging Neuroscience; Fluids and Barriers in the CNS. Reviewer for Acta Neuropathologica, Neuropathology and Applied Neurobiology, Clinical Anatomy, Experimental Neurology, Alzheimer's Society, Alzheimer's Research UK, EU Commission, Brain Canada. Member of British Neuropathological Society Academic Committee; Organising Committee Alzheimer's Disease International 2016, Pool of Experts BBSRC, Member of Alzheimer's Association International Society to Advance Alzheimer Research and Treatment (ISTAART) and Co-Chair Communications for Alliance of Women in Alzheimer's Research (AWARE). Brain Ageing Classification Working Group (2020-), Visiting Professor, University of Craiova, Romania, University of Targu Mures, Romania; Member Dept of Health COMEAP advisory committee on pollution effects on the brain. "La Caixa" Foundation Health Research Selection Committee - Neuroscience High Level Expert panel (2020), Scientific Expert Reviewer for Italian Ministry of Health and Romanian Ministry of Science and Health (2019, 2020). Rainwater Prize Committee (2019-); Future Leaders Fellowships Peer Review College (2019-); Editorial Board member Acta Neuropathologica Communications (2020-) Vice Chair of the Vascular Cognitive Disorders PIA Executive Committee of the Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART).

Leadership: Only European Committee Member for the USA National Plan to address Alzheimer's disease, NIH, 2016, 2019. Lead for the Interdisciplinary Dementia and Ageing Centre (IDeAC) University of Southampton, UK. Deputy Head of School of Clinical and Experimental Sciences, University of Southampton, Founder and lead for Clearance of Interstitial and Cerebrospinal Fluids (CLIC- Alzheimer's Association USA). Regional Lead for Deep Dementia Phenotyping (DEMON) Network. MRC Dementias Platform UK Vascular Experimental Medicine group. Vice Chair of the Vascular Cognitive Disorders PIA Executive Committee of the Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART); Chair of the Scientific Expertise team of Multiple Sclerosis Society, UK; Scientific Secretary of the British Neuropathological Society 2022-2024.

Prizes: Best research images at the 2011 Transmission Electron Microscopy British Society meeting; 2011 Ambassador's Prize for most accomplished Romanian Researcher in UK, Vice-Chancellor Award for Best Teacher, University of Southampton, 2013; Best poster (senior author) Alzheimer's Research UK 2014, 3rd prize poster Glia Magdeburg (Germany), 2014. Staff Achievement Award, University of Southampton 2014; best oral presentation British Association of Clinical Anatomists, 2015; Dementia Leader Award, Alzheimer's Society 2015, 1st prize Anatomical Society 2015, Venus Influential Woman of the Year 2016.

Consultancy: ROCHE pharmaceuticals, ALCYONE, ALNYLAM, Vaxxinity

Roles in Education

All levels of Anatomy teaching. Marker Intermediate and Finals Examinations. Programme Lead for the Masters in Medical Sciences, Faculty of Medicine, University of Southampton, 2010-2016. External Examiner, University of Sheffield, KCL, QMUL and Newcastle. Supervisor/co-supervisor for 8PhD students, 4MSc, 12MMedSc, 9BSc, 59BM5 project students. Securing on average £15,000 bursary funding for MMedSc students annually from British Neuropathological Society, Pathological Society, Anatomical Society. Advisor for PhD Students in Binghamton University, USA, University of Zurich, Switzerland, University of Lund, Sweden, University of Fukui, Japan, Vanderbilt University, USA.