R. Weissleder

*The author presented on this page has recently published his **10th article** since 2000 in Angewandte Chemie:* "Highly Magnetic Core–Shell Nanoparticles with a Unique Magnetization Mechanism": T.-J. Yoon, H. Lee, H. Shao, R. Weissleder, *Angew. Chem.* **2011**, *123*, 4759–4762; *Angew. Chem. Int. Ed.* **2011**, *50*, 4663–4666.

# Ralph Weissleder

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| **Date of birth:** | November 8, 1958 |
| **Position:** | Professor at Harvard University; Director at the Massachusetts General Hospital Center for Systems Biology (USA) |
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| **Education:** | 1979 Cand. med., University of Freiburg (Germany)<br>1985 MD, University of Heidelberg (Germany)<br>1986–1989 Postdoctoral fellow, Massachusetts General Hospital, Harvard Medical School (USA) |
| **Awards:** | **1990** President's Award, American Roentgen Ray Society; **1993** Memorial Award, American University Radiologists; **1993** Karl Decker Award; **2003** Achievement Award, Society for Molecular Imaging; **2003** Innovator in Medicine Award, Millennium Pharmaceuticals, Cambridge, Massachusetts; **2004** Allyn Taylor Award, Robarts Research Institute, London, Ontario; **2006** AMI Distinguished Basic Scientist Award; **2007** Gottfried-Wilhelm-Leibniz-Kette, German Society of Nuclear Medicine; **2008** RSNA Outstanding Researcher Award; **2009** Elected Member, National Academy of Science, Institute of Medicine; **2010** Gold Medal European Society of Radiology. |
| **Current research interests:** | The use of novel chemistries for imaging and for the quantitative measurement of human biology and drug effects in vivo. Current chemistry-related research areas include: bioorthogonal chemistries, nanomaterials, fluorochromes, smart sensors, radiopharmaceuticals, small-molecule inhibitors. |
| **Hobbies:** | Running, kayaking, hiking, rock climbing |

**What I look for first in a publication is …** the problem and then the data.

**If I won the lottery, I would …** continue doing science.

**The biggest problem that scientists face is …** explaining to the public what we do and why it's important.

**My favorite place on earth is …** my island.

**I chose chemistry as a career because …** I am an MD.

**My best investment was …** understanding my first chemistry kit at age 8.

**My secret/not-so-secret passion is …** chemistry.

**If I were not a scientist, I would be …** unemployed.

**My greatest achievement has been …** building my own house(s).

**The best stage in a scientist's career is …** dinner.

**Guaranteed to make me laugh is …** another paper rejection.

**I can never resist …** a nice long run.

**The downside of my job is …** dealing with the broken air conditioning.

**A good work day begins with …** writing a quick paper.

**When I'm frustrated, I …** either go run or write a paper.

**The most amusing chemistry adventure in my career was …** the aftermath of large quantities of wine to measure tannin levels (Jugend forscht 1976).

**My favorite author (fiction) is …** Jean-Paul Sartre.

**My top three films of all time are …** biofilm, filmy ferns (Hymenophyllaceae), and my film badge.

**My favorite style of music is …** merengue, at least this month.

***Has your approach to publishing your results changed since the start of your career?***

In the past 25 years of my research career, my approach to publishing has invariably changed. This is in part due to my changing research interests, the increasing availability of new technologies, and to a changing research environment, which is much more multidisciplinary today than it ever was before. What has remained unchanged, however, is my belief that all well-designed (and reproducible) research should be published. This approach allows results to be openly discussed, and ultimately serves to enhance our understanding of science. As a community, we will not advance if we fail to publish.

***What do you think the future holds for your field of research?***

Over the last two decades, I have seen extraordinary advances both in in vivo imaging and in the treatment of human diseases. These changes would have not been possible without applied chemistry. I am convinced that we are on the brink of another biotech revolution, in which the life sciences, engineering, and medicine will be merged and meaningfully integrated. This new "convergence" paradigm has already been adopted on various levels by several different institutions, and will likely lead to critical advances across many sectors (health, energy, food). In medicine particularly, this newly emerging scientific landscape holds the promise of important advances for patients.

**My 5 top papers:**

1. "Synthesis and In Vivo Imaging of a $^{18}$F-Labeled PARP1 Inhibitor Using a Chemically Orthogonal Scavenger-Assisted High-Performance Method": T. Reiner, E. J. Keliher, S. Earley, B. Marinelli, R. Weissleder, *Angew. Chem.* **2011**, *123*, 1963 – 1966; *Angew. Chem. Int. Ed.* **2011**, **50**, 1922 – 1925.
   This report describes a novel bioorthogonal labeling method for the rapid conversion of drugs into PET imaging agents. It is likely that the method will have a considerable impact on expediting the development of imaging probes for emerging drug targets. Using this approach, we were able to rapidly develop $^{18}$F-labeled probes for PARP-1 (Poly [ADP-ribose] polymerase 1), PLK1 (Polo-like kinase 1), Bcl-2 (B-cell lymphoma 2), CTSE (cathepsin E), EGFR (epidermal growth factor receptor), and PI3K (Phosphoinositide 3-kinase) among other cancer drug targets.
2. "Micro-NMR for Rapid Molecular Analysis of Human Tumor Samples": J. B. Haun, C. M. Castro, R. Wang, V. M. Peterson, B. S. Marinelli, H. Lee, R. Weissleder, *Sci. Transl. Med.* **2011** 3:71ra16.
   A long-held dream in medicine has been the capability for quick and accurate cancer diagnosis. Using an advanced NMR chip (originally described by us in *Nat. Med.* **2008**, *14*, 869 – 874, we performed the first prospective clinical trial, in which the protein expression levels from individual cancer patients could be detected using only small amounts of tumor tissue. Underlying this technology was the use of novel functionalized magnetic nanoparticles (*Angew. Chem.* **2011**, *123*, 4759 – 4762; *Angew. Chem. Int. Ed.* **2011**, *50*, 4663 – 4666) that were synthesized by a two-step bioorthogonal approach (*Nat. Nanotechnol.* **2010**, *5*, 660 – 665). This new technology has since opened up an entirely new avenue for monitoring cancer treatments; this landmark study received extensive press coverage.
3. "Cell-specific targeting of nanoparticles by multivalent attachment of small molecules": R. Weissleder, K. Kelly, E. Y. Sun, T. Shtatland, L. Josephson, *Nat. Biotechnol.* **2005**, *23*, 1418 – 1423.
   Nanomaterials with precise biological functions have considerable potential for use in biomedical applications. Herein, we investigated whether multivalent attachment of small molecules could increase the specific binding affinity and likewise reveal new biological properties of such nanomaterials. In this study, we described the parallel synthesis of a library that consists of 146 nanoparticles, each decorated with different synthetic small molecules. This research was integral in expanding the field of small-molecule targeting of nanomaterials.
4. "Magnetic relaxation switches capable of sensing molecular interactions": J. M. Perez, L. Josephson, T. O'Loughlin, D. Högemann, R. Weissleder, *Nat. Biotechnol.* **2002**, *20*, 816 – 820.
   Highly sensitive, efficient, and high-throughput biosensors are required not only for obtaining genomic and proteomic data from complex biological samples, but also potentially for in vivo applications. In this study, we developed biocompatible magnetic nanosensors that act as magnetic relaxation switches (MRS), detecting molecular interactions within the reversible self-assembly of disperse magnetic particles into stable nanoassemblies. Using four different types of molecular interactions (DNA – DNA, protein – protein, protein – small molecule, and enzyme reactions) as model systems, we showed that the MRS technology could detect these interactions with high efficiency and sensitivity using magnetic relaxation measurements such as magnetic resonance imaging (MRI). Furthermore, these magnetic changes were detectable in both turbid media and in whole-cell lysates without the need for protein purification.
5. "In vivo molecular target assessment of matrix metalloproteinase inhibition": C. Bremer, C.-H. Tung, R. Weissleder, *Nat. Med.* **2001**, 7, 743 – 748.
   A number of different matrix metalloproteinase (MMP) inhibitors have been developed as cytostatic and anti-angiogenic agents, and have undergone clinical testing. One major hurdle in assessing the efficacy of such drugs has been our inability to sense or image anti-proteinase activity directly and noninvasively in vivo. Herein, we showed that novel, biocompatible near-infrared fluorogenic MMP substrates could be used as activatable reporter probes for sensing MMP activity in intact tumors in nude mice. Moreover, we showed for the first time that using this approach, the effect of MMP inhibition could be directly imaged within hours of treatment initiation.

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