BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Goldberg, Alfred L.	Professor of Cell Biology
eRA COMMONS USER NAME	
AGOLDBERG	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Harvard University	A.B.	1963	Biochemistry
Cambridge University (England)		1963-1964	Physiology
Harvard Medical School		1964-1966	Medicine
Harvard University (GSAS)	Ph.D.	1968	Physiology

Positions and Employment

1968-1969 Postdoctoral Fellow of the National Research Council
1969-1971 Assistant Professor Physiology, Harvard Medical School
1976 Visiting Professor, University of California-Berkeley
1971-1977 Associate Professor of Physiology, Harvard Medical School
1977-1984 Professor of Physiology, Harvard Medical School
1984-1993 Professor of Molecular & Cellular Physiology, Harvard Medical School
1995 Visiting Professor, Institut Pasteur, University of Paris
1993- Professor of Cell Biology, Harvard Medical School

Honors. 1963 B.A, Magna cum laude, Phi Beta Kappa; 1963-64 Churchill Scholar, Cambridge Univ; 1969-71 Fellow, Med Foundation; 1970 Burroughs Lecturer, Univ. Iowa; 1972-77 Res. Career Develop. Award, NIH-; 1978 SKF Distinguished Lecturer; 1982 Disting Lecturer, Danish Acad. of Sciences; 1985-92 Member, Biogen Scientific Board; 1987-89 SAB FASEB Summer Conferences; 1989 Vice-Chairman & 1991 Chairman FASEB Conference "Ubiquitin & Protein Degradation"; 1990-91 Member, NIH-NSF Japanese Technology Evaluation Board; 1991 Panelist, NIH-NIAMSD Task Force; 1992-96 Chairman, ProScript, Inc. SAB; 1997 Panelist, FDA Advisory Board on Nutrition/Cachexia; F. McNaughton Prize Lecturer, McGill University-Montreal Neurological Inst; Symp. Organizer, 17th Intl Congress Biochem. San Francisco; 1998 Trustee, Wm. Townsend Porter Fdn; Novartis-Drew Univ. Award Biochemical Science (with T. Maniatis & A. Varshavsky); 1999 Rothchild Lecturer, Israel Acad. Sciences; Pfizer Lecturer, IRCM, Canada; 1999-2001SAB, Keystone Symposia; 2001 Plenary Lecture– Symposia Dystonia and Huntington's Disease Soc., 2002 Aventis-Nature Plenary Lecture; Leonardo da Vinci Lecture, Univ. Milan; 2003 Distinguished Lecturer NIEHS; Fay Memorial Lecturer, Univ. Mass Med School; Fellow, Ellison Foundation; Cachexia Society Special Symposia Honoring Dr. Goldberg's Pioneering Contributions; 2004 Severo Ochoa Prize, New York Univ; 2005 Nobel Lecturer, Karolinska Institute, Sweden; Fellow, American Academy Arts and Sciences; 2006 Centennial Lecturer, Biochemical Society; 2007, Pickart Plenary Lecturer, Keystone Meeting; Knobil Prize for Medical Research, Univ Texas School of Medicine (Houston); Pickart Plenary Lecturer (Keystone Meeting); Special Symposium honoring Dr. Goldberg's 65th Birthday "Ubiquitin and Protein Degradation" (Chinese Academy, Beijing); 2008 Plenary Lecturer FISEB Congress (Israel); and Internat Congress Cell Biology (Korea); 2008 CoOrganizer Banbury Conference "Growth & Atrophy of Muscle" (CSH, NY); Gabbay Award for Biotechnology and Medicine (Brandeis Univ); 2009 D.Sc (Honorary) Watson School of Biology (Cold Spring Harbor Laboratories); Elected Member, Institute of Medicine of the National Academies; Fellow, American Association for the Advancement of Science

Recent Publications (total articles -- 391 to date)

1. Rock, KL, York, IA, Saric, T, and **Goldberg, AL**. Protein degradation and the generation of MHC class I-presented peptides. Advances in Immunology 2001; 80: 1-70. PMCID: 12078479
2. **Goldberg, AL** and Rock, KL. Not just research tools–proteasome inhibitors offer therapeutic promise. Nature Medicine 2002; 8: 4, 338-340. PMCID: 11927937

3. Cascio, P, Call, M, Petre, BM, Walz, T, and **Goldberg, AL**. Properties of the hybrid form of the 26S proteasome containing both 19S and PA28 complexes. EMBO J; July 2002. PMCID: 12032076
4. Kandror, O, DeLeon, A, and **Goldberg, AL**. Trehalose synthesis is induced as a part of the cold shock response and is critical for cold-adaptation in E. coli. PNAS 2002; 99: 9727-9732. PMCID: 12105274
5. Benaroudj, N, Zwickl, P, Seemüller, E, Baumeister, W, and **Goldberg, AL**. ATP hydrolysis by the proteasome regulatory complex PAN serves multiple functions in protein degradation. Mol Cell 2003; 11: 69-78. PMCID: 12535522
6. Saric, T, Chang, S-C, Hattori, A, York, IA, Markant, S, Rock, K, Tsujimoto, M and **Goldberg, AL**. ERAP1, an interferon-γ-induced aminopeptidase in the endoplasmic reticulum, that trims precursors to MHC class I-presented peptides. Nature Immunology 2002; 3: 1169-1176. PMCID: 12436109
7. **Goldberg, AL**. Protein degradation and protection against misfolded..proteins. Nature 2003; 426: 895-899. PMCID: 14685250
8. Kandror, O, Bretschneider, N, Cavalieri, D, and **Goldberg, AL**. Yeast adapt to near-freezing temperatures by induction of trehalose synthesis and certain heat shock proteins. Mol Cell 2004; 13: 771-781. PMCID: 15053871
9. Venkatraman, P, Wetzel, R, Tanaka, M, Nukina, N, and **Goldberg, AL**. Eukaryotic proteasomes cannot digest polyglutamine sequences and must release them during degradation of polyglutamine-containing proteins. Mol Cell 2004; 14: 95-104. PMCID: 15068806
10. Sandri, M, Sandri, C, Gilbert, A, Skurk, C, Calabria, E, Picard, A, Walsh, K, Schiaffino, S, Lecker, SH, **Goldberg, AL**. Foxo transcription factors induce the atrophy-related ubiquitin ligase atrogin-1 and cause skeletal muscle atrophy. Cell 2004; 117: 399-412. PMCID: 15109499
11. Qiu, XB, Markant, S, and **Goldberg, AL**. Nrdp1-mediated degradation of the gigantic IAP, BRUCE, is a novel pathway for triggering apoptosis. EMBO J 2004; 23: 800-810. PMCID: 14765125
12. Rock, KL, York, I, **Goldberg, AL**. Post-proteasomal antigen processing for MHC class I presentation. Nature Immunology 2004; 5: 670-677. PMCID: 16181326
13. Chang, SC, Momburg, F, Bhutani, N and **Goldberg, AL**. The ER aminopeptidase, ERAP1, trims precursors to lengths of MHC class I peptides by a "molecular ruler" mechanism. PNAS 2005; 102: 17107-17112. PMCID: 16286653
14. Smith, D, Kafri, G, Cheng, Y, Ng, D, Walz, T and **Goldberg, AL**. ATP-binding (without hydrolysis) to PAN or the 19S ATPases causes association with the 20S proteasome, gate opening in the α-ring, and translocation of unfolded polypeptides. Mol Cell 2005; 20: 687-98. PMCID: 16337593
15. Kisselev, AF, Callard, A, and **Goldberg, AL**. Importance of different active sites in protein breakdown by 26S proteasomes and efficacy of proteasome inhibition depends on the protein substrate. J Biol Chem 2006; 281: 8582-8590. PMCID: 16455650
16. Sandri, M, Lin, L, Handschin, H, Yang, W, Arany, Z, Lecker, SH, **Goldberg, AL**, and Spiegelman, B. PGC-1a protects skeletal muscle from atrophy by suppressing FoxO3 action and atrophy-specific gene transcription. Proc Nat Acad Sci. 2006; 103:16260-5. PMCID: 17053067
17. Smith, D, Benaroudj, N, **Goldberg, AL**. Proteasomes and their associated ATPases: A destructive combination. J Structural Biol. 2006; 156:72-83. PMCID: 16919475
18. Bhutani, N, Venkatraman, P, and **Goldberg, AL**. Puromycin-sensitive aminopeptidase is responsible for digesting polyQ sequences released by proteasomes. EMBO J. 2007; 26: 1385-96. PMCID: 17318184
19. **Goldberg, AL**. Functions of the proteasome: from protein degradation and immune surveillance to cancer therapy. Biochem Soc Trans. 2007; 35:12-7. PMCID: 17212580
20. Smith, D, Chang, SC, Park, S, Finley, D, Cheng, Y, and **Goldberg, AL**. Docking of the proteasomal ATPases' C-termini in the 20S proteasomes α-ring opens the gate for substrate entry. Mol Cell. 2007; 27: 731-44. PMCID: 17803938
21. **Goldberg, AL**. On Prions, Proteasomes, and Mad Cows. N Engl J Med. 2007; 357: 1150-2. PMCID: 17855677
22. Zhao, J, Brault, JJ, Schild, A, Cao, P, Sandri, M, Schiaffino, S, Lecker, SH, and **Goldberg, AL**. FoxO3 Coordinately Activates Protein Degradation by the Autophagic (Lysosomal) and Proteasomal Pathways in Atrophying Muscle. Cell Metabolism. 2007; 6: 472-483. PMCID: 18054316
23. Rabl, J, Smith, DM, Yu, Y, Chang, SC, **Goldberg, AL**, and Cheng, Y. Mechanism of gate opening in the 20S proteasome by the proteasomal ATPases. Mol Cell. 2008; 30: 360-368. PMCID: 18471981

24. Medicherla, B and **Goldberg, AL**. Heat shock and oxygen radicals stimulate ubiquitin-dependent degradation mainly of newly synthesized proteins. J Cell Biol. 2008; 182: 663-7. PMCID: 18725537
25. Cohen, S, Gygi, SP, Glass, DJ, Valenzuela, D, Gartner, C, Brault, JJ, Latres, E, **Goldberg, AL**. During muscle atrophy, thick, but not thin, filament components are degraded by MuRF1-dependent ubiquitylation. J Cell Biol. 2009; 185: 1083-95. PMCID: 19506036

Ongoing Research Support

5 R01 GM51923-13 Goldberg (PI) **12/01/08-11/30/12**
NIH – NIGMS
Molecular Chaperones and Protein Degradation
These studies are attempting to understand the chaperone-like function of the proteasome-regulatory ATPases in controlling protein delivery to the 26S proteasome. Related studies are attempting to clarify how molecular chaperones, the stress-induced chemical chaperone, trehalose, and the ubiquitin-proteasome pathway collaborate in catalyzing the selective destruction of misfolded proteins.

1 R01 AR055255-01 Goldberg (PI) **09/25/08-06/30/13**
NIH
Molecular Mechanisms that Cause Muscle Atrophy
This research concerns the molecular mechanism for the excessive protein degradation in skeletal muscle seen in many catabolic states. (This grant is a continuation of a large grant funded by the National Space Biomedical Research Institute which no longer supports basic research.)

No Award Number Goldberg (PI) **7/01/08-6/30/10**
Multiple Myeloma Research Foundation
Novel Types of Proteasome Inhibitors
The proteasome active-site inhibitor Velcade (Bortezomib) is now widely used in the treatment of Multiple Myeloma and certain other lymphomas, and several other active-site inhibitors are in clinical trials. We are studying potential new targets in the proteasome that should allow development of novel inhibitors that may offer advantages in the clinic.

Completed Research Support

No Award Number Goldberg (PI) **1/01/09-12/31/09**
Johnson & Johnson
Identification of Agents that Activate or Inhibit Proteasomal Degradation

No Award Number Goldberg (PI) **1/01/07-12/31/09**
Muscular Dystrophy Association
Protein Breakdown in Muscle in Normal and Disease States
The objective of these studies is to define the biochemical mechanisms regulating rates of protein breakdown and proteasome activity in skeletal muscle, especially in dystrophic muscle.

No Award Number Goldberg (PI) **12/01/04-11/30/08**
Ellison Foundation (Senior Fellowship)
Regulation of Protein Degradation in Aging
The goal of this new grant is to analyze the functioning of the ubiquitin-proteasome pathway in neurons and in aging organisms, and specifically to understand how in various age-related diseases, there is an accumulation of and a failure to degrade misfolded proteins associated with neurodegeneration.

No Award Number Goldberg (PI) **11/01/05-10/31/07**
High Q Foundation
Cellular Metabolism of PolyQ Peptides
This grant supports a postdoctoral fellow to investigate the systems in neurons for degradation of Polyglutamine-containing proteins, which when expanded cause Huntington's Disease and related polyQ neurodenegereative diseases. These studies focus on the importance of proteasomal and lysosomal

(autophagic) systems in digesting polyQ proteins and the ability of different cellular peptidases to digest these sequences.