BIOGRAPHICAL SKETCH

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NAME: Ferrucci, Luigi

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

POSITION TITLE: Scientific Director, National Institute on Aging

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	FIELD OF STUDY
University of Florence Faculty of Medicine, Italy	M.D.	1974-1980	Medicine
University of Florence School of Gerontology	Geriatrics	1980-1984	Geriatric Medicine
Biology and Pathophysiology of Aging, University of Florence, Italy	Ph.D.	1985-1988	Predictors of Physical disability

A. Personal Statement

I am currently the Scientific Director of the National Institute on Aging. I am both an epidemiologist and geriatrician. My area of focus is on the disablement process in all of its multi-faceted aspects but especially the decline of physical function and mobility. Over the last 30 years, I have participated in designing, consolidating, analyzing, and publishing results from some of the largest epidemiological studies on aging performed in the United States and Europe. My current interest is studying the aging phenotypes, including changes in body composition, energetics, and use dysregulation and neurodegeneration as causes of frailty. My goal is to identify the biological and environmental mechanism that affect the speed of aging so that interventions can be identify that slow down the aging process, therefore preventing some of its negative consequences on physiology, pathology, physical and cognitive function, and quality of life.

B. Positions and Honors

1985 Geriatrician, at the INRCA (National Institute of Research and Care on Aging), Florence, Italy
1986 Geriatrician, Institute of Gerontology, University of Florence, Florence, Italy
1986 Associated Professor at the special School for Physical Therapists, University of Florence
1988-2002 Visiting Scientist and Visiting Associate at the Epidemiology, Demography and Biometry Program of the National Institute on Aging, NIH, Bethesda, Maryland (total 36 months)
Co-researcher in the Established Populations for Epidemiological Studies of the Elderly (EPESE). Analyses focused on understanding the disablement process and looking at new risk factors that affect longevity, active life expectancy, and morbidity
Co-investigator of the Women's Health and Aging Study, participating in the design and conduct of the study, and data management and analysis. Research activity focused on the multifactorial mechanisms by which specific diseases, comorbidity and impairments lead to disability in old age.
Principal Investigator of "InCHIANTI", a population based study of genetic, biological, environmental and socio-economical risk factors for mobility disability in older persons; sponsored by the Italian Ministry of Health and the Italian National Institute on Aging
Co-investigator of the Follow-up of the InCHIANTI study funded as a contract provided by the National Institute on Aging, National Institutes of Health
2003 NIA Staff Recognition Award, April 24, 2003

2003-2014 Chief, Longitudinal Studies Section Clinical Research Branch and Director of the BLSA, National Institute on Aging, Baltimore, MD
2004 NIA Staff Recognition Award, July 7, 2004
2005 NIH Directors Award for Excellence in Mentorship (Awarded July 14, 2005)
2005 DHHS NIH Recognition Certificate for personal and professional commitment to the education and training of students in the NIA 2005 Summer Research Training Program
2005-2011 Editor-in-Chief of the *Journal of Gerontology: Medical Sciences*
2008 NIH Directors Award, October 31, 2008
2008 Enrico Greppi Award, Societa Italiana di Geronotologie e Geriatria (Italian Society of Gerontology and Geriatrics), November 26, 2008
2009 Isico Award 2009 for "From chronic back pain to disability, a multifactorial mediated pathway: the InCHIANTI study" (Spine. 2001 Dec 15; 32(26):E809-15).
2009 St. Louis University's Max K. Horwitt Memorial Distinguished Lectureship Award, June 2, 2009
2010 NIH Plain Language and Clear Communication Bronze Award for the publication of "Healthy Aging: Lessons from the Baltimore Longitudinal Study of Aging May 26, 2010
2011-Present Scientific Director, National Institute on Aging
2011 Joseph T. Freeman Award from Gerontological Society of America (GSA), November 20, 2011
2011 Awarded the title of Honorary Member by the Board of Directors of the Italian Society of Gerontology and Geriatrics (SIGG), November 29, 2011
2013 NIH Director's Award, June 12, 2013
2014 Leadership in Aging Trailblazer Award, Maryland Governor's Award, May 15, 2014
2014 Longevity Prize of the Fondation IPSEN, November 6, 2014

C. Contribution to Science

C.1. My research has provided fundamental contributions to the notion that health in the older population is best assessed by functional status. I have developed some of the tolls to assess functional status in older persons that are now widely used both in research as well in clinical geriatrics. My research has demonstrated that information on functional status predicts disability, quality of life, health care expenditure, nursing home placement and mortality. In addition, my research has provided evidence that assessing mobility in a geriatric setting leads to a more effective care plan for older patients. BY studying the biological and clinical correlates of functional status with aging, I have also contributed to develop some of the mainstream hypothesis about causal pathways that lead to physical disability and mobility impairment with aging.

a. McDermott MM, Guralnik JM, Criqui MH, Liu K, Kibbe MR, Ferrucci L. Six-minute walk is a better outcome measure than treadmill walking tests in therapeutic trials of patients with peripheral artery disease. Circulation. 2014 Jul 1;130(1):61-8. doi: 10.1161/CIRCULATIONAHA.114.007002.
b. Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, Studenski S, Berkman LF, Wallace RB. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci. 2000 Apr;55(4):M221-31.
c. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med. 1995 Mar 2;332(9):556-61.
d. Cummings SR, Studenski S, Ferrucci L. A diagnosis of dismobility--giving mobility clinical visibility: a Mobility Working Group recommendation. JAMA. 2014 May;311(20):2061-2. doi: 10.1001/jama.2014.3033.

C.2. By leveraging my clinical experience as a geriatrician and epidemiological training I have developed an operational model of the physiological elements of the pathways that leads to disability in older persons, which include the central and peripheral nervous system, muscle, bone and joints, sensory input integration and energy production and utilization. This model has been implemented first in the InCHIANTI study and later in the reconceptualization of the Baltimore Longitudinal study of aging. By using data from these studies, I have described longitudinal trajectories of most of the phenotypes that change with aging including changes in body composition, energetics, homeostatic mechanisms and neurodegeneration/neuroplasticity and linked those trajectories to the development of physical and cognitive

impairments. I authored most of the work in the field demonstrating that muscle quality decline with aging and that muscle strength, rather than muscle mass, is the major predictor of disability with aging. This research has identified early biomarkers of impending disability that can be used in the evaluation of older patients.

a. Ferrucci L, Bandinelli S, Benvenuti E, Di Iorio A, Macchi C, Harris TB, Guralnik JM. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. J Am Geriatr Soc. 2000 Dec;48(12):1618-25.
b. Stenholm S, Shardell M, Bandinelli S, Guralnik JM, Ferrucci L. Physiological Factors Contributing to Mobility Loss Over 9 Years of Follow-Up-Results From the InCHIANTI Study. J Gerontol A Biol Sci Med Sci. 2015 May;70(5):591-7. doi: 10.1093/gerona/glv004. Epub 2015 Mar 7.

C.3. I have published the first report showing that the pro-inflammatory state of aging, operationalized as high level of circulating Interleukin-6 and C-reactive protein is a strong predictor of disability. In further work I demonstrated using multiple complementary approaches that up-regulation some inflammatory genes is a hallmark of aging and occur even in individuals free of risk factors and who are exceptionally healthy. I have demonstrated that, at least in part, the role of inflammation on disability is mediated by its deleterious effect on muscle mass and muscle strength. I have some state of the art mechanistic studies demonstrating that the pro-inflammatory state in an intrinsic characteristic of immune cells with chronic activation of the NF-KB system and is associated with down-regulation of adaptive immunity that cause blunted response to vaccination, susceptibility to infection and reduced ability to recover from it.

a. Ferrucci L, Harris TB, Guralnik JM, Tracy RP, Corti MC, Cohen HJ, Penninx B, Pahor M, Wallace R, Havlik RJ. Serum IL-6 level and the development of disability in older persons. J Am Geriatr Soc. 1999 Jun;47(6):639-46.
b. Ferrucci L, Corsi A, Lauretani F, Bandinelli S, Bartali B, Taub DD, Guralnik JM, Longo DL. The origins of age-related proinflammatory state. Blood. 2005 Mar 15;105(6):2294-9. Epub 2004 Nov 30.

C.4. I was part of the research group that first described the "unexplained anemia of aging", a clinical entity of unknown origin that represent 30% of the anemias after the age of 65 years. I authored most of the background work aimed at understanding the pathophysiology of this condition, including the role of blunted EPO production, reduced activity of the bone marrow, effect of inflammation on bone marrow response and, more recently, changes in erythrocytes survival. I published the first population-based study on the role of hepcidin in iron metabolism and anemia of chronic diseases.

a. **Ferrucci** L, Guralnik JM, Bandinelli S, Semba RD, Lauretani F, Corsi A, Ruggiero C, Ershler WB, Longo DL. Unexplained anaemia in older persons is characterised by low erythropoietin and low levels of pro-inflammatory markers. Br J Haematol. 2007 Mar;136(6):849-55.
b. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood. 2004 Oct 15;104(8):2263-8. Epub 2004 Jul 6.

C.5. I have done extensive studies on biomarkers of aging and chronic diseases, including studies on high throughput genetic, genomics, epigenetics and, recently, proteomics biomarkers. I have implemented the first epidemiological study that attempts to connect the theories of aging that have been developed in animal models to the phenotypes of aging in humans, both through direct measures of those hypothetical biological mechanism and high throughput biomarkers. This research is aimed at understanding the biological mechanism of aging which implies high susceptibility to chronic multimorbidity and disability.

a. Lin H, Joehanes R, Pilling LC, Dupuis J, Lunetta KL, Ying SX, Benjamin EJ, Hernandez D, Singleton A, Melzer D, Munson PJ, Levy D, Ferrucci L, Murabito JM. Whole blood gene expression and interleukin-6 levels. Genomics. 2014 Dec;104(6 Pt B):490-5. doi: 10.1016/j.ygeno.2014.10.003. Epub 2014 Oct 13.

My Bibliography URL (1,032 citations):

http://www.ncbi.nlm.nih.gov/sites/myncbi/1DogihU4e2B/bibliography/47683120/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

Because I work in the NIH intramural program, my only source of support is the Intramural program.

Completed Research Support

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