

# Stanford

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## Leonore A. Herzenberg

Department of Genetics Flow Cytometry Professor

### CONTACT INFORMATION

- **Alternate Contact**

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### Bio

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### ACADEMIC APPOINTMENTS

- Professor (Research), Genetics

### ADMINISTRATIVE APPOINTMENTS

- Endowed Chair of Flow Cytometry and Genetics, Stanford University, (2015- present)

### HONORS AND AWARDS

- Honorary Fellow, Royal Microscopical Society (2016)
- Visionary use of Information Technology in the field of Medicine, Torino Medical Science Award, (2007)
- "for contributions to the work for which the Kyoto Prize was awarded", United States presentation of the Kyoto Prize (2006)
- Heroic Achievement in Information Technology, The ComputerWorld Smithsonian Award (1996)
- Eleanor Roosevelt Cancer Fellowship,, American Cancer Society (1986)
- Symposium Chair & Speaker, International Congress of Immunology (1986)
- Member, Genetics Society of America (0)
- Member, American Association of Immunologists (0)

### PROFESSIONAL EDUCATION

- D.Sc-equiv., University Paris V Sorbonne , Immunolgy (1981)

### PATENTS

- Leonore Herzenberg, David Parks, Stephen Meehan, Wayne Moore. "United States System and Methods for Selecting a Multiparameter Reagent Combination for Automated Fluorescence Compensations", Leland Stanford Junior University, May 20, 2014
- Wayne Moore, David R. Parks, Leonore A. Herzenberg. "United States Patent 8,548,950 Method and system for data archiving", The Board Of Trustees Of The Leland Stanford Junior University, Oct 1, 2013
- Leonard A. Herzenberg, Leonore A. Herzenberg, Stephen C. De Rosa, James Andrus,. "United States Patent 7,723,389 N-acetylcysteine compositions and methods for the treatment and prevention of drug toxicity", The Board Of Trustees Of The Leland Stanford Junior University, May 25, 2010

- Parks, D.R., Bryan, V.M., Herzenberg, L.A.. "United States Patent 4,667,830 Cell labeling with antigen-coupled microspheres", Leland Stanford Junior University, May 26, 2002
- Roederer, M., Rabin, R., Herzenberg, L.A., Herzenberg, L.A.. "United States Patent 5,968,755 Methods for Determining T-cell Profiles of Immunocompromised Subjects", Leland Stanford Junior University, Oct 29, 1999
- Herzenberg, L.A., De Rosa, S.C, Herzenberg, L.A. and Roederer, M.. "United States Patent 5,843,785 Glutathione Deficiency as a prognosis for survival in AIDS", Leland Stanford Junior University, Dec 1, 1998
- Herzenberg, L.A., Herzenberg, L.A.. "United States Patent 5,580,577 Method of treating the symptoms of human rhinovirus infection", Leland Stanford Junior University, Dec 3, 1996
- Nolan, G.P., Feiring, S, Herzenberg, L.A.. "United States Patent 5,070,012 Monitoring of cells and trans-activating transcription elements", Leland Stanford Junior University, Dec 3, 1991
- Steinman, L., Waldor, M.K., Sriram, S., Herzenberg, L.A., Herzenberg, L.A.. "United States Patent 4,695,459 Method of treating autoimmune diseases that are mediated by LEU3/CD4 phenotype T cells.", Leland Stanford Junior University, Sep 22, 1987
- Wulf Droge, Leonard A. Herzenberg, Leonore A. Herzenberg. "United States Patent 5,607,974 Treatment of diseases associated with cysteine deficiency", The Board Of Trustees Of The Leland Stanford Junior University, Mar 4, 0097
- Wulf Droge, Leonard A. Herzenberg, Leonore A. Herzenberg. "United States Patent 1,339.256 Treatment of diseases associated with hiv-infections", The Board Of Trustees Of The Leland Stanford Junior University, Jan 26, 0089
- Antonio Hardan, Rabindra Tirouvanziam, Leonore A. Herzenberg. "United States Patent 2,846,789 Compositions and methods for treating autism and autism spectrum disorder", The Board Of Trustees Of The Leland Stanford Junior University, May 3, 0012
- Denong Wang, Leonore A. Herzenberg, Donna M. Peehl, Leonard A. Herzenberg. "United States Patent 7,981,625 PROSTATE CANCER GLYCAN MARKERS AND AUTOANTIBODY SIGNATURES", The Board Of Trustees Of The Leland Stanford Junior University, Jul 19, 0011
- Leonard A. Herzenberg, David Rhodes Parks, Leonore A. Herzenberg, Wayne A. Moore, Vernon T. Oi. "United States Patent 6,947,953 Internet-linked system for directory protocol based data storage, retrieval and analysis", The Board Of Trustees Of The Leland Stanford Junior University, Sep 20, 0005

## LINKS

- Laboratory Website: <http://herzenberglab.stanford.edu>
- Our Facebook Page: <https://www.facebook.com/LAHerzenberg>
- Herzenberg Laboratory - YouTube: <https://www.youtube.com/user/herzenberglab>

## Research & Scholarship

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### CURRENT RESEARCH AND SCHOLARLY INTERESTS

Our laboratory focuses on understanding the basic mechanisms that determine and regulate gene expression and cell function in the immune system. Most recently, we have distinguished two functionally and physically distinct murine B cell lineages, only one of which (B-2) originates with the traditional bone marrow HSC and displays the well known characteristics of B cells that develop from the continuously renewed HSC in adult bone marrow. The other lineage, B-1a, develops from phenotypically distinct progenitors that are only detectable during fetal and early neonatal life and give rise to mature B-1a cells that develop de novo during the first 6-8 weeks of life and persist thereafter by division of the mature B cells.

Consistent with these life-style differences, our extensive IgH sequencing studies demonstrate that the antibody repertoires expressed by the two B cell lineages are shaped by forces that operate at different times during development, i.e., the B-1a repertoire is shaped by rearrangements that occur during fetal and neonatal life and are propagated by cell division thereafter, whereas the B-2 repertoire begins to develop around weaning (>6 weeks of age) and continues de novo development from HSC throughout life.

As might be expected from these decidedly distinct life styles, B-1a and B-2 show overlapping but clearly distinct IgH repertoire differences. B-1a have long known to be the source of many "anti-self" ("natural") antibodies as well as many antibodies reactive with many microorganisms. Intriguingly, we find very little difference (<10%) between the B-1a repertoire obtained from germ-free mice versus that obtained from conventionally-reared mice, indicating that exposure to self antigen conditions the B-1a anti-bacterial repertoire rather than vice versa.

In addition to our B cell studies, our laboratory maintains a strong interest in intracellular redox influences in health and disease. In earlier work, we showed that as HIV infection progresses, intracellular glutathione (GSH) levels decrease, resulting ultimately in severe intracellular GSH deficiency. Excessive acetaminophen (Tylenol) use also results in severe GSH deficiency due to GSH consumption during acetaminophen detoxification. N-acetylcysteine (NAC), a non-toxic source of cysteine, is the accepted antidote for GSH depletion. We have established flow cytometry assays for evaluating GSH depletion and its repletion by N-acetylcysteine and continue to explore the medical consequences of GSH depletion.

These and many other biomedical findings rely heavily on cell analysis and sorting with the Fluorescence-Activated Cell Sorting (FACS), which our laboratory developed initially and to which we continually add new software and hardware functionality. The dedicated group of engineers, physicists, statisticians, mathematicians, computer scientists and programmers in our FACS development group continues to make leading edge contributions to flow technology. Most recently, we developed new, user friendly and statistically reliable software to facilitate flow data analysis. We are making this software available free of charge to laboratories at .edu, .org, and similar non-profit institutions.

Overall, our laboratory operates as a community of scholars working in diverse but inter-related areas. We tend to be highly collaborative and often have students and fellows from other laboratories working at our benches. We are always open to new collaborations and new students and fellows interested in genetics, molecular biology, immunology, cell biology and/or in technology development related to these areas.

## Teaching

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### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Genetics (Phd Program)
- Immunology (Phd Program)

## Publications

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### PUBLICATIONS

- **Science not art: statistically sound methods for identifying subsets in multi-dimensional flow and mass cytometry data sets** *NATURE REVIEWS IMMUNOLOGY*  
Orlova, D. Y., Herzenberg, L. A., Walther, G.  
2018; 18 (1): 77-+
- **AutoGate: automating analysis of flow cytometry data.** *Immunologic research*  
Meehan, S., Walther, G., Moore, W., Orlova, D., Meehan, C., Parks, D., Ghosn, E., Philips, M., Mitsunaga, E., Waters, J., Kantor, A., Okamura, R., Owumi, et al  
2014; 58 (2-3): 218-223
- **The early history of Stanford Immunology.** *Immunologic research*  
Jones, P. P., Herzenberg, L. A.  
2014; 58 (2-3): 164-178
- **A Conversation with Leonard and Leonore Herzenberg** *ANNUAL REVIEW OF PHYSIOLOGY, VOL 76*  
Herzenberg, L. A., Herzenberg, L. A., Roederer, M.  
2014; 76: 1-20
- **Our NIH Years: A Confluence of Beginnings** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
Herzenberg, L. A., Herzenberg, L. A.  
2013; 288 (1): 687-702
- **A MULTI-CENTER, PHASE IIB, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF THE EFFECTS OF N-ACETYLCYSTEINE (NAC) ON REDOX CHANGES AND LUNG INFLAMMATION IN CYSTIC FIBROSIS PATIENTS**  
Tirouvanziam, R., Lymp, J., Thompson, V., CHATFIELD, B. A., Nicholls, D., Clancy, J. P., Vender, R., Egan, M., Quittell, L., Michelson, P., Antony, V., Spahr, J., Rubenstein, et al

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- **Automatic clustering of flow cytometry data with density-based merging.** *Advances in bioinformatics*  
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2009; 686759-?
- **Modern flow cytometry: A practical approach** *CLINICS IN LABORATORY MEDICINE*  
Tung, J. W., Heydari, K., Tirouvanziam, R., Parks, D. R., Herzenberg, L. A., Herzenberg, L. A.  
2007; 27 (3): 453-?
- **N-Acetylcysteine - a safe antidote for cysteine/glutathione deficiency** *CURRENT OPINION IN PHARMACOLOGY*  
Atkuri, K. R., Mantovani, J. J., Herzenberg, L. A., Herzenberg, L. A.  
2007; 7 (4): 355-359
- **Epitope-specific regulation: the elephant in the bathtub** *NATURE IMMUNOLOGY*  
Herzenberg, L. A.  
2007; 8 (8): 783-786
- **Interpreting flow cytometry data: a guide for the perplexed** *NATURE IMMUNOLOGY*  
Herzenberg, L. A., Tung, J., Moore, W. A., Herzenberg, L. A., Parks, D. R.  
2006; 7 (7): 681-685
- **B cell lineages: documented at last!** *NATURE IMMUNOLOGY*  
Herzenberg, L. A., Tung, J. W.  
2006; 7 (3): 225-226
- **Genetics, facts, immunology, and redox: A tale of two lives intertwined** *ANNUAL REVIEW OF IMMUNOLOGY*  
Herzenberg, L. A., Herzenberg, L. A.  
2004; 22: 1-31
- **IL-6 Signaling Mediates the Germinal Center Response, IgM Production and Nociceptive Sensitization in Male Mice after Tibia Fracture.** *Brain, behavior, and immunity*  
Li, W., Yang, Y., Guo, T., Sahbaie, P., Shi, X., Guang, Q., Kingery, W. S., Herzenberg, L. A., David Clark, J.  
2021
- **CTLA-4 expression by B-1a B cells is essential for immune tolerance.** *Nature communications*  
Yang, Y. n., Li, X. n., Ma, Z. n., Wang, C. n., Yang, Q. n., Byrne-Steele, M. n., Hong, R. n., Min, Q. n., Zhou, G. n., Cheng, Y. n., Qin, G. n., Youngyunpipatkul, J. V., Wing, et al  
2021; 12 (1): 525
- **The class II peptide editor, H2-M, affects the development and repertoire of B-1 cells**  
Ghosh, D., Pham, T. D., He, X., O'mara, M. E., Kantor, A. B., Khoa Nguyen, Sengupta, D., Eisenlohr, L. C., Jensen, P. E., Herzenberg, L. A., Boyd, S. D., Ghosn, E. B., Mellins, E. D.  
AMER ASSOC IMMUNOLOGISTS.2020
- **Germinal Center Formation, Immunoglobulin Production and Hindlimb Nociceptive Sensitization after Tibia Fracture.** *Brain, behavior, and immunity*  
Li, W. W., Yang, Y. n., Shi, X. Y., Guo, T. Z., Guang, Q. n., Kingery, W. S., Herzenberg, L. A., David Clark, J. n.  
2020
- **Automated subset identification and characterization pipeline for multidimensional flow and mass cytometry data clustering and visualization.** *Communications biology*  
Meehan, S., Kolyagin, G. A., Parks, D., Youngyunpipatkul, J., Herzenberg, L. A., Walther, G., Ghosn, E. E., Orlova, D. Y.  
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- **Hematopoietic stem cell-independent hematopoiesis and the origins of innate-like B lymphocytes.** *Development (Cambridge, England)*  
Ghosn, E. n., Yoshimoto, M. n., Nakauchi, H. n., Weissman, I. L., Herzenberg, L. A.  
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- **Automated subset identification and characterization pipeline for multidimensional flow and mass cytometry data clustering and visualization.** *Communications biology*  
Meehan, S., Kolyagin, G. A., Parks, D., Youngyunpipatkul, J., Herzenberg, L. A., Walther, G., Ghosn, E. E., Orlova, D. Y.

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- **Omentum immune microenvironment: Metastatic niche for ovarian cancer**  
Krishnan, V., Raju, P. A., Vierkoetter, K., Patel, S., Youngyunpatkul, J., Tallapragada, S., Schaar, B., Folkins, A. K., Herzenberg, L. A., Dorigo, O.  
AMER ASSOC CANCER RESEARCH.2018
- **HSC-requirement for macrophage regeneration is tissue-specific**  
Ghosn, E., Kuipers, H., Waters, J., Sosa, J., Phillips, M., Herzenberg, L. A.  
AMER ASSOC IMMUNOLOGISTS.2018
- **QFMatch: multidimensional flow and mass cytometry samples alignment** *SCIENTIFIC REPORTS*  
Orlova, D. Y., Meehan, S., Parks, D., Moore, W. A., Meehan, C., Zhao, Q., Ghosn, E. B., Herzenberg, L. A., Walther, G.  
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- **Evidence for altered levels of IgD in the nasal airway mucosa of patients with chronic rhinosinusitis** *JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY*  
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- **Basophil activation test determination of CD63 combined with CD203c is not superior to CD203c alone in identifying allergic bronchopulmonary aspergillosis in cystic fibrosis.** *The Journal of allergy and clinical immunology*  
Gernez, Y., Waters, J., Tirouvanziam, R., Herzenberg, L., Moss, R.  
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- **Characterization of immunoglobulin E plasma cells that are elevated in the upper airway mucosa of nonatopic patients with chronic rhinosinusitis without nasal polyps** *INTERNATIONAL FORUM OF ALLERGY & RHINOLOGY*  
Rashan, A. R., Ghosn, E., Peterson, A., Yang, Y., Phillips, M., Sahaf, B., Herzenberg, L., Nayak, J. V.  
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- **Fetal Hematopoietic Stem Cell Transplantation Fails to Fully Regenerate the B-Lymphocyte Compartment** *STEM CELL REPORTS*  
Ghosn, E. E., Waters, J., Phillips, M., Yamamoto, R., Long, B. R., Yang, Y., Gerstein, R., Stoddart, C. A., Nakauchi, H., Herzenberg, L. A.  
2016; 6 (1): 137-149
- **Fetal Hematopoietic Stem Cell Transplantation Fails to Fully Regenerate the B-Lymphocyte Compartment.** *Stem cell reports*  
Ghosn, E. E., Waters, J., Phillips, M., Yamamoto, R., Long, B. R., Yang, Y., Gerstein, R., Stoddart, C. A., Nakauchi, H., Herzenberg, L. A.  
2016; 6 (1): 137-149
- **Blood basophil activation is a reliable biomarker of allergic bronchopulmonary aspergillosis in cystic fibrosis** *EUROPEAN RESPIRATORY JOURNAL*  
Gernez, Y., Walters, J., Mirkovic, B., Lavelle, G. M., Colleen, D. E., Davies, Z. A., Everson, C., Tirouvanziam, R., Silver, E., Wallenstein, S., Chotirmall, S. H., McElvaney, N. G., Herzenberg, et al  
2016; 47 (1): 177-185
- **Basophil activation test determination of CD63 combined with CD203c is not superior to CD203c alone in identifying ABPA in cystic fibrosis** *Journal of Allergy and Clinical Immunology*  
Gernez, Y., Waters, J., Tirouvanziam, R., Herzenberg, L. A., Moss, R. B.  
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- **Earth Mover's Distance (EMD): A True Metric for Comparing Biomarker Expression Levels in Cell Populations.** *PloS one*  
Orlova, D. Y., Zimmerman, N., Meehan, S., Meehan, C., Waters, J., Ghosn, E. E., Filatenkov, A., Kolyagin, G. A., Gernez, Y., Tsuda, S., Moore, W., Moss, R. B., Herzenberg, et al  
2016; 11 (3)
- **Amyloid fibrils activate B-1a lymphocytes to ameliorate inflammatory brain disease** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
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2015; 112 (49): 15016-15023
- **Blood basophil activation is a reliable biomarker of allergic bronchopulmonary aspergillosis in cystic fibrosis.** *The European respiratory journal*  
Gernez, Y., Walters, J., Mirkovi#, B., Lavelle, G. M., Colleen, D. E., Davies, Z. A., Everson, C., Tirouvanziam, R., Silver, E., Wallenstein, S., Chotirmall, S. H., McElvaney, N. G., Herzenberg, et al

2015

- **Co-administration of N-Acetylcysteine and Acetaminophen Efficiently Blocks Acetaminophen Toxicity.** *Drug development research*  
Owumi, S. E., Andrus, J. P., Herzenberg, L. A., Herzenberg, L. A.  
2015; 76 (5): 251-258
- **Co-administration of N-Acetylcysteine and Acetaminophen Efficiently Blocks Acetaminophen Toxicity** *DRUG DEVELOPMENT RESEARCH*  
Owumi, S. E., Andrus, J. P., Herzenberg, L. A., Herzenberg, L. A.  
2015; 76 (5): 251-258
- **Long-term treatment with oral N-acetylcysteine: Affects lung function but not sputum inflammation in cystic fibrosis subjects. A phase II randomized placebo-controlled trial** *JOURNAL OF CYSTIC FIBROSIS*  
Conrad, C., Lymp, J., Thompson, V., Dunn, C., DAVIES, Z., CHATFIELD, B., Nichols, D., Clancy, J., Vender, R., Egan, M. E., Quittell, L., Michelson, P., Antony, et al  
2015; 14 (2): 219-227
- **Cysteine Oxidation Targets Peroxiredoxins 1 and 2 for Exosomal Release through a Novel Mechanism of Redox-Dependent Secretion** *MOLECULAR MEDICINE*  
Mullen, L., Hanschmann, E., Lillig, C. H., Herzenberg, L. A., Ghezzi, P.  
2015; 21
- **Layered evolution in the immune system: a view from history** *B-1 CELL DEVELOPMENT AND FUNCTION*  
Herzenberg, L. A.  
2015; 1362: 1-5
- **B-1 Cell Development and Function** *B-1 CELL DEVELOPMENT AND FUNCTION*  
Rothstein, T. L., Herzenberg, L. A., Holodick, N. E., Ghosn, E.  
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- **Demonstration That Antigen-Binding Cells Are Precursors of Antibody-Producing Cells After Purification with a Fluorescence-Activated Cell Sorter** *JOURNAL OF IMMUNOLOGY*  
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- **Linkage of inflammation and oxidative stress via release of glutathionylated peroxiredoxin-2, which acts as a danger signal** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
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- **Selective uptake of single-walled carbon nanotubes by circulating monocytes for enhanced tumour delivery.** *Nature nanotechnology*  
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Smith, B. R., Ghosn, E. E., et al  
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- **Metabolic Adaptation of Neutrophils in Cystic Fibrosis Airways Involves Distinct Shifts in Nutrient Transporter Expression** *JOURNAL OF IMMUNOLOGY*  
Laval, J., Touhami, J., Herzenberg, L. A., Conrad, C., Taylor, N., Battini, J., Sitbon, M., Tirouvanziam, R.  
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- **Blastocyst complementation generates exogenic pancreas in vivo in apancreatic cloned pigs** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
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- **H-Y antigen-binding B cells develop in male recipients of female hematopoietic cells and associate with chronic graft vs. host disease** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Sahaf, B., Yang, Y., Arai, S., Herzenberg, L. A., Herzenberg, L. A., Miklos, D. B.  
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- **Blood basophils from cystic fibrosis patients with allergic bronchopulmonary aspergillosis are primed and hyper-responsive to stimulation by aspergillus allergens** *JOURNAL OF CYSTIC FIBROSIS*  
Gernez, Y., Dunn, C. E., Everson, C., Mitsunaga, E., Gudiputi, L., Krasinska, K., Davies, Z. A., Herzenberg, L. A., Tirouvanziam, R., Moss, R. B.  
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- **Reversal of Paralysis and Reduced Inflammation from Peripheral Administration of beta-Amyloid in T(H)1 and T(H)17 Versions of Experimental Autoimmune Encephalomyelitis** *SCIENCE TRANSLATIONAL MEDICINE*  
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- **A Randomized Controlled Pilot Trial of Oral N-Acetylcysteine in Children with Autism** *BIOLOGICAL PSYCHIATRY*  
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Gernez, Y., Tirouvanziam, R., Reshamwala, N., Yu, G., Weldon, B. C., Galli, S. J., Herzenberg, L. A., Nadeau, K. C.  
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