CURRICULUM VITAE

RACHEL A. ALTURA, M.D.

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EDUCATION

Undergraduate:

Brandeis University
Biochemistry and Biology
B.A. 1984-1988

Medical School:

Washington University School of Medicine, 1988-1992, M.D. 1992

POSTGRADUATE TRAINING

Residency:

St. Louis Children's Hospital-Washington University School of Medicine
Internship and Residency in Pediatrics, 1992-1995

Fellowship:

St. Jude Children's Research Hospital, Memphis, Tennessee
Fellowship in Pediatric Hematology-Oncology, 1995-1999

POST GRADUATE HONORS AND AWARDS

Awards

Bio-Ohio: Top 30 Researchers in their 30s, 2007
Honorary Master of Arts, Brown University, 2009
U.S. News and World Report Top Oncology Doctor, 2011-2012

PROFESSIONAL LICENSES AND BOARD CERTIFICATION

American Board of Pediatrics, 2002-2014
American Board of Pediatrics, sub-board Pediatric Hematology-Oncology, 2004-2014

ACADEMIC APPOINTMENTS

Associate Professor 2008-present
Department of Pediatrics,
The Warren Albert Medical School at Brown University
Providence, RI

Principal Investigator, 2007-present
Department of Pediatrics
Rhode Island Hospital
Providence, RI

Assistant Professor, 2007-2008
Department of Pediatrics,
The Warren Albert Medical School at Brown University
Providence, RI

Assistant Professor, 1999-2007
Department of Pediatrics,
The Ohio State University School of Medicine & Public Health,
Children's Hospital, Columbus, Ohio,

Principal Investigator, 2002-2007
Center for Childhood Cancer,
Columbus Children's Research Institute, Columbus, OH

HOSPITAL APPOINTMENTS

Hasbro Children's Hospital 2007-
Attending Physician, Hematology/Oncology

Women & Infants Hospital
Consulting physician, Pediatric Hematology/Oncology 2008-

Columbus Children's Hospital
Attending Physician, Hematology/Oncology 1999-2007

MEMBERSHIP IN SOCIETIES

American Association for Cancer Research
Children's Oncology Group

Society for Pediatric Research

SENIOR EDITOR

International Journal of Biochemistry and Molecular Biology	2011-2012

AD HOC REVIEWER

Cancer Research	2003-2012
Oncogene	2003-2008
EMBO	2003-2008
EMBO Reviews	2003-2008
American Journal of Pathology	2003-2011
Molecular Cancer Therapeutics	2003-2010
Clinical Cancer Research	2003-2008
Neuropathology and Applied Neurobiology	2003-2008
International Journal of Cancer	2003-2008
Journal of Cellular and Molecular Medicine	2003-2008
Molecular Cancer	2003-2008
Cellular and Molecular Life Sciences	2003-2008
Brain Research	2003-2008
Human Molecular Genetics	2003-2008
Nature Cancer Reviews	2008
Endocrine-Related Cancer	2010-2011
Molecular Medicine	2010
Experimental Dermatology	2010-2011
FASEB Journal	2011
Diabetologia	2012

PUBLICATIONS

1. Jencks, W.P., **Altura, RA.** The perils of carbonic acid equilibrium constants. **Journal of Chemical Education***,* 65: 770-771, 1988.
2. Al**tura, R.A.,** Rymond, B., Seraphin, B., Rosbash, M. Sequence requirements for branch formation in a Group II self-splicing intron. **Nucleic Acids Research***,* 17: 335-354, 1989.
3. **Altura, R.A.,** Valentine, M., Li, H., Boyett, J.M., Shearer, P., Grundy, P., Shapiro, D.N., Look, A.T. Identification of novel regions of deletion in familial Wilms tumor by comparative genomic hybridization. **Cancer Research***,* 56: 3837-3841, 1996.
4. **Altura, R.A**., Maris, J.M., Li, H., Boyett, J.M., Brodeur, G.M., Look, A.T. Novel regions of chromosomal loss in familial neuroblastoma by comparative genomic hybridization. **Genes, Chromosomes, and Cancer***,* 19:176-184, 1997.
5. **Altura, R.A., Inukai**, T., Ashmun, R.A., Zambetti, G.P., Roussel, M.F., Look, A.T. The chimeric E2A-HLF transcription factor abrogates p53-induced apoptosis in myeloid leukemia cells. **Blood***,* 92: 1397-1405, 1998.
6. **Altura, R.A.,** Head, D.R., Wang, W.C. Long-term survival in infants with idiopathic myelodysplasia. **Br. J. Heme***,* 109: 459-462, 2000.
7. **Altura, R.A.,** Wang, W.C., Wynn, L., Altura, B.M., Altura, B.T. Hydroxyurea therapy associated with declining serum levels of magnesium in children with sickle cell anemia. **J. Pediatrics***, 140: 565-9, 2002.*
8. Saavedra, H.I., Maiti, B., Timmers, C., **Altura, R.,** Tokuyama, Y., Fukasawa, K., Leone, G. Inactivation of E2F3 results in centrosome amplification. **Cancer Cell***,* 2 (3): 333-346, 2003.

9. **Altura, R.A.,** Olshevski, R.S., Boue, D.B. Nuclear expression of Survivin in pediatric ependymomas and choroid plexus tumors correlates with morphologic tumor grade **Br J Cancer**, 89: 1743-1749, 2003.
10. Fangusaro, J., Klopfenstein, K., Groner, J., Hammond, S., **Altura, R.A.** Inflammatory myofibroblastic tumor following bone marrow transplantation: report of two pediatric cases **Bone Marrow Transplant,** 33 (1): 103-107, 2004.
11. Jiang, Y., Saavedra, H.I., Holloway, M.P., Leone, G., **Altura, R.A.** Regulation of survivin by the Rb/E2F pathway. **J Biol Chem***,* 279: 40511-20, 2004.
12. Zehtabchi, S., Sinert, R., Rinnert, S., Chang, B., Heinis, C**., Altura, R.A.,** Altura, B.T.A, Altura, B.M. Serum ionized magesium levels and ionized calcium-to-magnesium ratios in adult patients with sickle-cell anemia. **Am J Hematology**, 77(3): 215-22, 2004.
13. Fangusaro, J.R., Jiang, Y., Holloway, M.P., Caldas, H., Singh, V., Boué, D.R., Hayes, J., **Altura, R.A.** Survivin, Survivin-2B and Survivin-deltaEx3 Expression in Medulloblastoma: Biologic Markers of Tumor Morphology and Clinical Outcome. **Br J Cancer***,* 92: 359-365, 2005.
14. Caldas, H., Jiang, Y., Holloway, M.P., Mahotka, C., Fangusaro, J., Conway, E.M., **Altura, R.A.** Survivin Splice Variants Regulate the Balance Between Proliferation and Cell Death. **Oncogene**, 24 (12):1994-2007, March 2005.
15. Caldas, H., Honsey, L., **Altura, R.A.** Survivin 2α: A Novel Survivin Splice Variant Expressed in Malignancies. **Molecular Cancer**, 4(1):11, March 2005.
16. Jiang, Y., De Bruin, A., Caldas, H., Fangusaro, J., Hayes, J., Conway, E.M., Robinson, M.L., **Altura, R.A.** Essential role for survivin in early brain development. **J Neuroscience**, 25 (30): 6962-70, July 2005.
17. Caldas, H., Holloway, M.P., Hall, B., Qualman, S., **Altura, R.A.** Survivin-directed short-interfering RNA cocktail is a potent suppressor of tumor growth in vivo. **J Med Genetics**, 43(2):119-28, Feb 2006.
18. Fangusaro, J.R., Caldas, H., Jiang, Y., **Altura, R.A.** Survivin, an inhibitor of apoptosis in pediatric cancer. **Pediatric Blood and Cancer** ;47(1):4-13, July 2006.
19. Caldas, H., Jaynes, F.O., Boyer, M.W., Hammond, S., **Altura, R.A.** Survivin and Granzyme B-Induced Apoptosis (SAGA), a Novel Anticancer Therapy. **Mol Can Therapeutics**, 5(3): 693-703, 2006.
20. Caldas, H., Fangusaro, J.R., Boue, D.R., Holloway, M.P., **Altura, R.A.** Dissecting the role of Endothelial Survivin Variants in Angiogenesis. **Blood**, 109: 1479-1489, Feb 2007.
21. Zwerts. F., Lupu, F., De Vriese, A., Pollefeyt, A., Moons, L., **Altura, R.A.,** Jiang, Y., Maxwell, P., Hill, P., Oh, H., Rieker, C., Collen, D., Conway, S.J., Conway, E.M. Lack of endothelial cell survivin during embryonic development causes defects in angiogenesis and neural tube closure. **Blood**, 109 (11):4742-52, Jun 2007.
22. Jiang Y, Nishimura W, Devor-Henneman D, Kusewitt D, Wang H, Holloway MP, Dohi T, Robinson ML, Sharma A, Altieri D, and **Altura RA**. Postnatal expansion of the pancreatic β-cell mass is dependent on survivin. **Diabetes.** 57(10):2718-27. October, 2008.
23. Kelly MJ, Meloni-Ehrig AM, Manley PE, and **Altura RA**. Poor outcome in a pediatric patient with acute myeloid leukemia associated with a variant t(8;21) and trisomy 6. **Cancer Genetics and Cytogenetics***,* 189(1):48-52. Feb 2009.
24. Kelly M, Martin L, Alonso M, and **Altura RA**. Liver transplant for relapsed undifferentiated embryonal sarcoma in a young child. **Journal of Pediatric Surgery**, e1-3, Dec 2009.
25. Kurosawa H, Okuya M, Kikuchi J, Furukawa Y, Matsui H, Inykai T, Goto H, **Altura RA**, Sugita K, Look AT, and Inaba T. Upregulation of survivin by the E2A-HLF

chimera is indispensable for the survival of t(17;19)-positive leukemia cells, **Journal of Biological Chemistry**, 285(3):1850-60. Jan 15 2010.

26. Samkari A, Borzutky A, Treaba D, Dedeoglu F, and **Altura RA**. Novel Mutation in MVK Associated with MK Deficiency and Dyserythropoeitic Anemia. **Pediatrics** 125(4):e964-8. Apr 2010.
27. Wang H, Gambosova K, Cooper ZA, Holloway MP, Kassai A, Izquierdo D, Cleveland K, Boney C, and **Altura RA.** EGF regulates survivin stability through the Raf-1/ERK pathway in insulin-secreting pancreatic beta-cells. **BMC Molecular Biology**, 11:66, 2010.
28. Wang H, Holloway MP (co-first author), Ma L, Cooper ZA, Riolo M, Samkari A, Elenitoba-Johnson K, Chin YE, and **Altura RA**. Acetylation directs Survivin nuclear localization to repress STAT3 oncogenic activity. **Journal of Biological Chemistry**, 285(46):36129-37. PMID: 20826784. 2010 Nov 12; Epub 2010 Sep 8.
29. Invited Review special issue: **Current Pediatric Reviews: Apoptosis in Pediatric Disorders***.* Ayman Samkari and **Rachel A. Altura.** Inhibition of Apoptosis in Pediatric Cancer by Survivin, 7 (4):277-284, 2011.
30. Samkari A, Cooper ZA, Holloway MP, Liu J and **Altura RA**. Rapamycin induces the anti-apoptotic protein survivin in neuroblastoma. **Int J Biochem Mol Biol.** 2012;3(1):28-35. Epub 2012 Feb 10.
31. Yakirevich E, Samkari A, Holloway MP, Lu S, Singh K, Yu J, Fenton MA & **Altura RA**. *(*2011). Survivin and Acetylated Survivin Correlate with Distinct Molecular Subtypes of Breast Cancer. Human Pathology*,* PMID: 22055399.
32. Riolo MT, Cooper ZA, Holloway MP, Bianchi C, Yakirevich E, Ma L, Chin YE & **Altura RA**. (2012) Histone Deacetylase 6 (HDAC6) Deacetylates Survivin for its Nuclear Export in Breast Cancer. Journal of Biological Chemistry, 287(14):10885-93. PMID: 22334690*.*
33. Nguyen KT, Holloway MP, & **Altura RA**. The CRM1 nuclear export protein in normal development and disease. (2012) International Journal of Biochemistry and Molecular Biology, 3(2):137-151. PMID: 22773955.
34. Holloway MP & **Altura RA**. (2012) Targeting survivin's co-conspirators: do alternative methods of trapping survivin in the nucleus have potential in triple negative breast cancer**. Future Oncology**, 8(8): 907-909.
35. Miranda CJ, Braun L, Jiang Y, Hester MH, Zhang L, Riolo M, Wang H, Rao M, **Altura RA** & Kaspar BK. (2012). Aging brain microenvironment decreases hippocampal neurogenesis through wnt-mediated Survivin signaling. **Aging Cell** 11(3): 542-52. PMID:22404871*.*

ABSTRACTS

1. **Altura, R.,** Rymond, B., Seraphin, B., Rosbash, M. The 5' end of the intron suppresses hydrolysis of Group II 5' splice sites. Platform Presentation, Meeting on RNA Processing, Cold Spring Harbor Laboratories, 1988.
2. **Altura, R.A**., DeCou, J., Valentine, M., Shearer, P., Look, A.T., Boyett, J.M., Shapiro, D.N. Chromosomal regions containing new candidate oncogenes and tumor suppressors in Wilms tumor detected by comparative genomic hybridization. Platform Presentation, American Pediatric Society-Society for Pediatric Research, Washington D.C., 1996.
3. **Altura, R.A.**, Inukai, T., Zambetti, G.P., Roussel, Look, A.T. The chimeric E2A-HLF transcription factor abrogates p53-induced apoptosis in myeloid leukemia cells.

Simultaneous Session: Oncogenes I The American Society of Hematology, 39th Annual Meeting, 1997.

4. **Altura, R.A.,** Head, D.R., Wang, W.C. Prolonged survival of children with idiopathic myelofibrosis. 41st Annual Meeting of The American Society of Hematology, 1999.
5. **Altura, R.**, Timmers, C., Sang, L., Gustavo, L., Regulation of Survivin Gene Expression By the E2F Family of Transcription Factors. 43rd Annual Meeting of American Society of Hematology, 2001
6. **Altura, R.A.**, Olshefski, R.S., Jiang, Y., Boué, D.R. Expression of Survivin in normal brain and in corresponding pediatric CNS tumors. Society for Neuro-Oncology, 2003.
7. **Altura, R.A**., Holloway, M.H., Blumenkrantz, M., Anderson, J.R., Qualman, S.J., Leone, G. Expression of survivin in alveolar rhabdomyosarcoma predicts outcome. American Association of Cancer Research, 2004.
8. Fangusaro, J., Jiang, Y., Boue, D., **Altura, R.A.** Expression of survivin, survivin-2B, and survivin delta-exon3 in medulloblastoma. International Symposium on Pediatric Neuro-Oncology, 2004.
9. Caldas, H., Jiang, Y., **Altura, R.A.** Alternative survivin—based therapies for medulloblastoma. Third International Meeting on Targeted Therapies for Cancer. August 2004.
10. Caldas, H., **Altura, R.A.** Survivin-Mediated Suicide Gene Therapy for Malignant Tumors. 19th Annual Meeting of the International Society for Biological Therapy of Cancer (iSBTc). November 2004.
11. Jiang, Y., Caldas, H., de Bruin, A., Fangusaro, J., Conway, E.M., Robinson, M.R., **Altura, R.A.** Survivin is essential for the survival and maintenance of neurons within the mammalian CNS and PNS, Keystone Symposium, Cellular Senescence and Cell Death (J7-2005), March 2005.
12. Caldas, H., Holloway, M.P., Hall, B.M., **Altura, R.A.** RNA interference of multiple survivin isoforms is a potent tumor growth suppressor in vivo. Platform Presentation, American Association for Cancer Research, 96th Annual Meeting, 2005, Experimental Therapeutics Section.
13. Caldas, H., Sasser, K., Hall, B.M., **Altura, R.A.** Efficacy and safety of SAGA in the treatment of breast cancer. American Association for Cancer Research, 96th Annual Meeting, 2005, Experimental Therapeutics Section.
14. Jiang, Y., Caldas, H., de Bruin, A., Fangusaro, J., Conway, E.M., Robinson, M., **Altura, R.A.** Survivin is essential for the survival and maintenance of the mammalian nervous system. Platform Presentation, 2005 Pediatric Academic Society, Developmental Biology Session.
15. Jiang, Y., de Bruin, A., Caldas, H., Conway, E.M., Robinson, M., **Altura, R.A.** Survivin is essential for early brain development. Society for Neuroscience, 2005.
16. Caldas, H., Fangusaro, J., Boue, D., Holloway, P., **Altura, R.A.** Role of Survivin-deltaexon3 in angiogenesis. Experimental Biology/FASEB, 2006.
17. Robinson, M.L., Jiang, Y., Murtagh, D.S., Conway, E.M., **Altura, R.A.** Defective lens development in the absence of survivin. Platform presentation. ARVO, 2006.
18. Jiang, Y., Devor-Henneman, D., Kusewitt, D.F., Yin, H., Robinson, M.R., **Altura, R.A.** Survivin regulates β□cell mass after birth. ADA Research Symposium- Translating islet biology into diabetes therapy. March, 2007. Platform presentation.
19. Maiti, B., Jiang, Y., Holloway, M.P., **Altura, R.A.** Survivin is essential for proliferation and collaborates with c-myc in the transformation of mouse embryonic fibroblasts. Keystone Symposium- March, 2007.
20. Y Jiang, W Nishimura, T Dohi, M Holloway, H Wang, M Robinson, A Sharma, D Altieri, and **R Altura**. The cancer-associated gene, survivin, is required for the

postnatal expansion of pancreatic beta-cells. Platform Presentation. Pediatric Academic Societies' & Asian Society for Pediatric Research Joint Meeting 2008.
21. Miranda C, Jiang Y, Braun L, Rao M, **Altura RA**, Kaspar BK. Aging environment alters neural progenitor cell proliferation. Platform Presentation. Society for Neuroscience, 2008.
22. Kassai A, Wang H, Holloway M, and **Altura RA**. High Fat and High Carbohydrate Diets Markedly Accelerate Diabetes in Mice Lacking Survivin. Platform Presentation. American Diabetes Association, June 2009.
23. Matthew Riolo, Katelyn Soares, and **Rachel Altura**. Differential regulation of survivin by reactive oxygen species in breast cancer cells. AACR Conference on Frontiers in Basic Cancer Research. October, 2009.
24. Michael Holloway, Haijuan Wang, Li Ma, Kojo Elenitoba-Johnson, Eugene Chin, and **Rachel Altura**. Acetylated Survivin Represses STAT3 Enhanceosome Activity. American Association for Cancer Research, 101st Annual Meeting, 2010.
25. Zachary A. Cooper, Matthew Riolo, Michael P. Holloway, **Rachel A. Altura**. Acetylated Survivin functions in DNA damage repair. 102nd AACR Annual Meeting, April 2011.
26. Evgeny Yakirevich, Shaolei Lu, Ayman Samkari, Kamaljeet Singh, Michael Holloway, **Rachel A. Altura**. Survivin and acetylated Survivin predict outcome in breast cancer and correlate separately with a basallike and luminal-type expression profile. 102nd AACR Annual Meeting, April 2011.
27. Ayman Samkari, Zachery Cooper, Michael P Holloway, **Rachel A. Altura**. Rapamycin induces the anti-apoptotic protein Survivin in high-risk neuroblastoma by enhancing its interaction with HSP90. 24th annual meeting of the American Society of Pediatric Hematology/Oncology, April 2011
28. Michael P Holloway, Bradley D DeNardo, Qinqin Ji, Marcus B. Valentine, Jill Lahti, Arthur Salomon and **Rachel A Altura**. Quantitative phosphoproteomics identifies activation of the RET and IGF-1R/IR signaling pathways in N-MYC amplified neuroblastoma. American Association of Cancer research-Japanese Cancer Association, February 2013.
29. Y Cheng PhD, MP Holloway PhD, K Nguyen, MG Kauffman MD PhD, S Shacham PhD and **RA Altura** MD. Inhibition of the nuclear transport protein CRM1 induces human breast cancer cell death by regulating survivin degradation. American Association of Cancer Research Annual Meeting, April 2013.

OTHER MEDIA

T.V. News story- Columbus Children's Research Institute Discovers Selective Target to Suppress Tumor Growth- 6/15/05

On-line press release: Protein 'jailbreak' helps cancer cells live- HealthCanal.com, R&D Magazine, PhysOrg.com, News-Medical.net, news.brown.edu- March 28, 2012

INVITED REVIEWS

1. Current Pediatrics, special edition Apoptosis in Pediatric Disorders. Ayman Samkari and **Rachel A. Altura.** Inhibition of Apoptosis in Pediatric Cancer by Survivin, Nov 2011.
2. McGraw-Hill Yearbook of Science & Technology, Biochemistry and Molecular Biology Section, STAT3, December 2011

GRANTS

ACTIVE:

Hyundai Hope on Wheels
PI: Altura
Title: Identifying the phosphoproteome in high- and low-risk neuroblastoma tumors.
The goal of this project is to identify novel phosphoproteomic signatures in primary high-risk neuroblastoma tumors that can be used for both prognostic and therapeutic targets.

COBRE Center for Cancer Research Development
P20RR017695-06A2
Project Principal Investigator: Altura
Title: Post-translational modification of survivin: a novel therapeutic approach for cancer
The goal of this project is to characterize the function of acetylated survivin in cancer.

Karyopharm Therapeutics
PI: Altura
Title: Role for CRM1 inhibitors in blocking survivin and STAT3 pathways
The goal of this collaboration is to characterize several nuclear export inhibitors that are entering clinical trials.

INTELLECTUAL PROPERTY

Apoptosis-inducing genes for treating cancer. U.S. Patent No. 8,017,747.