ISABEL ALICIA LÜTHY

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Date of birth: August 13th, 1954.
Place of birth: Buenos Aires, Argentina.
Marital status: married, 1 child

Educational Training:

Pre-doctoral: Bachelor in Sciences, Chemistry. Faculty of Exact and Natural Sciences, Universidad Nacional de Buenos Aires, 1978.

Ph.D.: Ph.D. in Chemistry. Thesis: "Hormonal regulation on Sex Steroid Hormones and Prolactin Receptors in the adrenal gland". Department of Biological Chemistry, Faculty of Exact and Natural Sciences, Universidad Nacional de Buenos Aires. Presented on 12-20-1983. Suma cum laude.

Post-doctoral: Centre de Recherches en Endocrinologie Moléculaire, Centre Hospitalier de l'Université Laval, Québec, Canada, with Professor Fernand Labrie (1984-1988).

A. Positions and Honors.

Positions and employment

1) Auxiliar teacher, Department of Biological Chemistry, Faculty of Exact and Natural Sciences, National University of Buenos Aires: September 1978-February 1979.
2) Fellow from the Argentine National Research Council in the "Instituto de Biología y Medicina Experimental": 1979-1984.
3) Two months work in the "Abteilung für Klinische Chemie", Max-Planck Institut für Psychiatrie, Munich, Germany, under the direction of Dr. Karl Martin Pirke: January-March 1981.
4) Post-doctoral Fellow from the Argentine National Research Council in the Centre de Recherches en Endocrinologie Moléculaire, Québec, Canadá: 1984-1987.
5) Auxiliar teacher, Laval University in the Molecular Endocrinology Laboratory, Québec, Canada, 1987-1988.
6) Associated Researcher from the Argentine National Research Council in the "Instituto de Biología y Medicina Experimental": 1992-1996.
7) Fellowship from the "International Cancer Technology Transfer Fellowships (ICRETT), administered by the "International Union Against Cancer" (UICC) in the Molecular Endocrinology Laboratory, "Centre de Recherches du Centre Hospitalier de l'Université Laval", Québec, Canada, December 1999.
8) Independient Researcher from the Argentine National Research Council (CONICET) in the "Instituto de Biología y Medicina Experimental": 97 – 2012.
9) Principal Investigator from the Argentine National Research Council (CONICET) in the "Instituto de Biología y Medicina Experimental": 2013 - .

Patent :

USA Invention Patent. Title: "Mouse Mammary tumor lines expressing estrogen and progeste-

rone receptors". Lanari, C., Molinolo, A.A., **Lüthy, I.A.** N° 6,808,924, 26 October 2004.

Other experience and professional memberships

Member of the Directive Committee of the following Societies:

1. Argentine Society for Clinical Research: (1991) and Secretary: 1999.
2. Argentine Biology Society (1994 - 2006), President: 2005 and 2006.
3. Titular member of the Directive Committee of the Argentine Association for the Advancement of Sciences (2002 - 2008).

Honors

1) CEDIQUIFA Award in Pharmacoloy 1994 (Center for Studies of the Development of Chemical-Pharmaceutical Industry in Argentina to the research team of the "Instituto de Biología y Medicina Experimental", April 1994.
2) Accesit Award "Florencio I. Fiorini" for the work "Regulatory mechanisms in carcinogenesis induced by progestins", Molinolo A, Kordon E, Montecchia MF, Pazos P, Dran G, **Lüthy IA**, Lanari C, November 1995.
3) Oncology Foundation "Encuentro": November 2000.
4) "Eugenia Sacerdote de Lustig" award for the work "Expression of epithelial cadherin and related proteins in IBH-6 and IBH-4 human breast cancer cell lines". Lapyckyj L, Matos ML, Castillo LF, Gabrielli NM, **Lüthy IA**, Vázquez-Levin MH, september 2009.
5) "Eugenia Sacerdote de Lustig" award for the work "Regulation of cell proliferation and tumor growth in breast cancer models by α_2- et β_2-adrenoceptors". C Pérez Piñero, A Bruzzone, LF Castillo, **IA Lüthy**, september 2010.

B. Peer-reviewed publications (in chronological order).

1) Nuclear steroid binding in rat adrenal gland. RS Calandra, LME Finocchiaro, **IA Lüthy**, RN Cheb-Terrab. Acta Physiol. latinoamer. 30: 333-336, 1980.
2) Influence of sex and gonadectomy on sex steroid receptors in rat adrenal gland. RS Calandra, **IA Lüthy**, LME Finocchiaro, RN Cheb-Terrab. J. Steroid Biochem. 13: 1331-1333, 1980.
3) Specific prolactin binding in the rat adrenal gland: its characterization and hormonal regulation. JC Calvo, LME Finocchiaro, **I Lüthy**, EH Charreau, RS Calandra, B Enstrom, V Hansson. J.Endocrinol. 89: 317-325, 1981.
4) Influence of starvation on the dihydrotestosterone-luteinizing hormone feedback in the male rat. KM Pirke, JL Barañao, R Calandra, **I Lüthy**, B Spyra. J. Ster. Biochem. 16: 403-406, 1982.
5) Effects of prolactin, bromocriptine and sulpiride on estrogen and lactogenic receptors in the rat adrenal gland. **IA Lüthy**, VA Chiauzzi, EH Charreau, RS Calandra. Acta Physiol. pharmacol. latinoamer. 34: 15-23, 1984.
6) Prolactin regulation of prolactin binding sites in pancreatic islets and adrenal glands of ovariectomized rats. M Tesone, **IA Lüthy**, RG Ladenheim, RS Calandra, EH Charreau. J. Receptor Res. 3: 711-726, 1983-84.
7) Ontogeny of sex steroid and prolactin receptors in the male rat adrenal gland. **IA Lüthy**, RS Calandra. Experientia 40: 1002-1004, 1984.
8) Prolactin binding sites in the brain and kidneys of the toad Bufo arenarum Hensel. **IA Lüthy**, ET Segura, VI Lüthy, EH Charreau, RS Calandra. J. Comp. Physiol B 155: 611- 614, 1985.
9) Effect of median eminence lesions and hormonal replacement on the prolactin receptors in the adrenal gland and Langerhans islets from ovariectomized adult rats. **IA Lüthy**, M Tesone, RM Oliveira-Filho, GM Somoza, EH Charreau, C Libertun, RS Calandra. J.Receptor Res. 5: 105-119, 1985.
10) Bromocriptine and sulpiride competitively inhibit estrogen binding to its receptor in the adrenal gland. **IA Lüthy**, RS Calandra. Experientia 42: 136138, 1896.

11) Characteristics of interaction of the antiandrogen flutamide with the androgen receptor in various target tissues. J Simard, **I Lüthy**, J Guay, A Bélanger, F Labrie. Mol. Cell. Endocrinol. 44: 261-270, 1986.
12) Development of androgen resistance in mouse mammary tumor cells can be prevented by the antiandrogen flutamide. **I Lüthy**, F Labrie. The Prostate 10: 89-94, 1987.
13) Flutamide in combination with castration (surgical or medical) is the standard treatment in advanced prostate cancer. F Labrie, A Dupont, A Bélanger, J Emond, G Monfette, **I Lüthy**, J Simard, R Lachance. J Drug Develop. 1: Supplement 1: 34-51, 1987.
14) Effect of flutamide, a pure antiandrogen, on the pituitary-ovarian axis in the adult female rat. **I Lüthy**, S Caron, A Bélanger, F Labrie. Gynecol. Endocrinol. 1: 151-168, 1987.
15) Combination therapy in stage C and D prostatic cancer: rationale and 5-year clinical experience. Labrie F, Dupont A, Bélanger A, Cusan L, Giguère M, Lacourcière Y, **Luthy I**, Bégin D, Labrie C, Simard J, Monfette G, Edmond J. Cancer and Metastatic Reviews, 6: 615-636, 1987.
16) Adrenal precursor C_{19} steroids are potent stimulators of growth of androgen-sensitive mouse mammary carcinoma Shionogi cells "in vitro". Bégin D, **Luthy IA,** Labrie F. Mol.Cell. Endocrinol 58: 213-219, 1988.
17) Mediation by the androgen receptor of the stimulatory and antiandrogenic actions of 17ß-estradiol on the growth of androgen-sensitive Shionogi mammary carcinoma cells in culture. **Luthy I**, Bégin D, Labrie F. Endocrinology 123: 1418-1424, 1988.
18) Androgenic activity of synthetic progestins and spironolactone in androgen-sensitive mouse mammary carcinoma (Shionogi) cells in culture. **IA Lüthy**, DJ Bégin, F Labrie. J. Ster. Biochem. 31: 845-852, 1988.
19) Effects of hyperprolactinemia on ornithine decarboxylase activity and polyamine levels in seminal vesicles of genetically prolactin-deficient adult dwarf mice. Gonzalez SI, Chandrashekar V, Shire JGM, **Luthy IA**, Bartke A, Calandra RS. Biology of Reproduction 44: 321-326, 1991.
20) Effect of medroxyprogesterone acetate (MPA) and serum factors on cell proliferation in primary cultures of an MPA-induced mammary adenocarcinoma. Dran G, **Luthy IA**, Molinolo AA, Montecchia F, Charreau EH, Dosne Pasqualini C, Lanari C. Breast Cancer Reasearch and Treatment 35: 173-186, 1995.
21) Atypical androgen receptor in the human melanoma cell line IIB-MEL-J. Morvillo V, **Luthy IA**, Bravo AI, Capurro MI, Donaldson M, Quintans C, Calandra RS, Mordoh J. Pigment Cell Research, 8: 135-141, 1995.
22) Prazosin and stress effect on tumoral growth of 7,12-dimethylbenz[a]anthracene-induced rat mammary tumors. Wendel V, Vázquez SM, Durante P, Lemoine A, Segura E, Calandra RS, **Luthy IA**. Acta Physiologica, Phamacologica et Therapeutica Latinoamericana 46: 277-285, 1996.
23) Binding of ^{125}I-Prolactin to spermatozoa from normospermic and asthenospermic men. **Luthy IA**, Mormandi E, Aszpis S, Vázquez SM, Maccallini G, Levalle O, Calandra RS. J. Endocrinological Investigation 20 : 635-639, 1997.
24) Progesterone receptor involvement in independent tumor growth in MPA-induced murine mammary adenocarcinomas. Montecchia MF, Lamb C, Molinolo AA, **Luthy IA**, Pazos P, Lanari C. J. Ster. Biochem. Mol. Biol. 68 : 11-21, 1999.
25) α_2-Adrenergic Effect On Human Breast Cancer MCF-7 Cells. Vazquez S; Pignataro O, **Luthy IA**. Breast Cancer Research and Treatment 55: 41-49, 1999.
26) Five novel hormone responsive cell lines derived from murine mammary ductal carcinomas. *In vivo* and *in vitro* effects of estrogen and progestins. Lanari C, **Lüthy IA**, Lamb CA, Fabris V, Pagano E, Helguero L, Sanjuan N, Merani S, Molinolo AA. Cancer Research 61: 293-302, 2001.
27) Androgen receptors in human melanoma cell lines IIB-MEL-LES and IIB-MEL-IAN and in human melanoma metastases. Morvillo V, **Lüthy IA**, Bravo AI, Capurro MI, Portela P, Calandra RS, Mordoh J. Melanoma Research 12 (6): 529-38, 2002.
28) Augmented serum levels of the IGF-I/IGFBP3 ratio in pre-menopausal patients with type I breast cysts. Enriori P, Fischer C, Gori J, Etkin A, Calandra RS, **Lüthy IA.** European Journal of Endocrinology 148 (2): 177-184, 2003.
29) Three Novel Hormone-Responsive Cell Lines Derived from Primary Human Breast Carcinomas. Functional Characterization. Vázquez SM, Mladovan AG, Garbovesky C, Baldi A, **Lüthy IA.** Journal of Cellular Physiology 199 (3): 460-469, 2004.

30) Breast cyst fluids increase proliferation of breast cell lines in correlation with their content of hormones and growth factors. Enriori P, Vázquez SM, Chiauzzi V, Pérez C, Fischer CR, Gori JR, Etkin AE, Charreau EH, Calandra RS, **Lüthy, IA.** Clinical Endocrinology 64(1): 20-28, 2006.
31) Human breast cell lines exhibit functional α_2-Adrenergic Receptors. Vázquez SM, Mladovan AG, Pérez C, Bruzzone A, Baldi A, **Lüthy IA**. Cancer Chemotherapy and Pharmacology 58: 50-61, 2006.
32) Contribution of alpha2-adrenoceptors to the mitogenic effect of catecholestrogen in human breast cancer MCF-7 cells. Chiesa IJ, Castillo LF, **Lüthy IA**. Journal of Steroid Biochemistry and Molecular Biology 110 (1-2): 170-185, 2008. (pISSN: 0960-0760).
33) α_2-Adrenergic action on cell proliferation and mammary tumour growth in mice. Bruzzone A, Pérez Piñero C, Castillo LF, Sarappa MG, Rojas P, Lanari C, Lüthy IA. British Journal of Pharmacology 155 (4): 494-504, 2008. (pISSN: 0007-1188).
34) Novel Human Breast Cancer Cell Lines IBH-4, IBH-6 and IBH-7 Growing in Nude Mice. Bruzzone A, Vanzulli S, Soldati R, Giulianelli S, Lanari C, **Lüthy IA.** Journal of Cellular Physiology 219: 477- 484, 2009. (pISSN: 0021-9541).
35) Adrenoceptors: Non Conventional Target for Breast Cancer? **Lüthy IA**, Bruzzone A, Pérez Piñero C, Chiesa I, Castillo L, Vázquez SM. Current Medicinal Chemistry 16(15): 1850-62, 2009. (ISSN: 0929-8673).
36) Expression analysis of Epithelial Cadherin and related Proteins in IBH-6 and IBH-4 Human Breast Cancer Cell Lines. Lapyckyj L, Castillo LF, Matos ML, Gabrielli NM, **Lüthy IA**, Vazquez-Levin MH. Journal of Cellular Physiology 222: 596-605, 2010. (pISSN: 0021-9541).
37) Classical and non-classical membrane progesterone receptors in murine mammary carcinomas: Agonistic effects of progestins and antiprogestins mediating rapid non-genomic effects. Bottino M, Rojas P, Soldati R, Mondillo C, Pignataro O, Calvo J, Gutkind JS, Amornphimoltham P, Molinolo A, **Lüthy I**, Lanari C. Breast Cancer Research and Treatment 2010 (in press) (pISSN: 0167-6806).
38) α_2-adrenoceptors enhance cell proliferation and mammary tumour growth in both the stroma and the tumor cells". A. Bruzzone*, C. Pérez Piñero*, P. Rojas, C. Lanari and **I.A. Lüthy**. En révision au Current Cancer Drug Targets. *équal participation. Current Cancer Drug Targets 11:763-774, 2011.
39) Involvement of α_2- and β_2-adrenoceptors on breast cancer cell proliferation and tumour growth regulation", C. Pérez Piñero, A. Bruzzone, M.G. Sarappa, L.F. Castillo, **I.A. Lüthy**. British Journal of Pharmacology 166 (2): 721-736, 2012.
40) Adrenergic action in breast cancer. **Lüthy IA**, Bruzzone A, Pérez Piñero C. Current Cancer Therapy Reviews 8: 90-99, 2012. (Review in the especial volume: "The adrenergic axis in Cancer").
41) PI3K/AKT pathway regulates the ligand-independent activation of steroid receptors, hormone independence and tumor differentiation in breast cancer. Riggio M, Polo ML, Blaustein M, Colman Lerner A, **Lüthy I**, Lanari C, Novaro V. Carcinogenesis 33 (3): 509-518, 2012.

Chapters of books:

1) Prolactin effects on the prepubertal male rat. JL Barañao, M Tesone, JC Calvo, **IA Lüthy**, SI Gonzalez, EH Charreau, RS Calandra. In: "Recent advances in male reproduction: molecular basis and clinical implications". Eds: A. Mongioi & R D'Agata, Raven Press, New York, 7: 305-312, 1983.
2) New concepts on the androgen sensitivity of prostate cancer. F Labrie, **I Lüthy**, R Veilleux, J Simard, A Bélanger, A Dupont. In: Second Int. Symposium on Prostate Cancer (Murphy G, S Khoury, ed), Alan Liss Inc. New York. pp 145-172, 1987.
3) Rationale for maximal androgen withdrawal in the therapy of prostate cancer. Labrie F, Bélanger A, Veilleux R, Lacoste D, Labrie C, Marchetti B, Poulin R, Dupont A, Cusan L, **Luthy I**. In: Baillière's Clinical Oncology on Prostatic Cancer (Furr BAJ, Denis L. eds), Saunders Company, London, Nov. 1988. p. 597-619.
4) Combination therapy with the antiandrogen Flutamide and the LHRH agonist [D-Trp^6, des-Gly-NH_2^{10}]LHRH ethylamide in prostate cancer: rationale and 5-year clinical experience. Labrie F, Dupont A, Bélanger A, Simard J, Labrie C, Poulin R, **Luthy I**, Veilleux R, Lacoste D,

Marchetti B, Cusan L, Manhès G, Monfette G, Emond J. In: Molecular biology of Brain and Endocrine Peptidergic Systems (Mc Kerns KW, ed), Montréal, 1988, pp 83-101.

5) Pathogenesis of ductal and lobular progestin-induced mammary carcinomas in BALB/c mice. Molinolo AA, Pazos P, Montecchia F, Kordon EC, Dran G, Guerra F, Elizalde P, **Luthy I**, Charreu EH, Pasqualini CD, Lanari C. In: Hormonal Carcinogenesis II. (Li JJ, Li SA, Nandi S, Gustafsson JA, Sekely LI, eds). Springer, New York, pp: 141-147, 1996.
6) Hormonas. Mecanismos de acción hormonal. Gonadotrofinas y Prolactina. **IA Lüthy**, SI Gonzalez-Calvar, RS Calandra. In CD-Rom: "Andrología. Fisiopatología y Clínica". Ed: Oscar Levalle, Buenos Aires, 2002.
7) Hormonas esteroideas. **IA Lüthy.** En Fisiopatología Endocrina: bioquímica y métodos diagnósticos. Ed: MA Pisarev, RS Calandra, MO Suescun, GJ Juvenal. Fascículo II, Montpellier, 2004. ISSN 1515-3878.

International meeting presentations: 22.

National Argentine, Canadian or French meeting Presentations: 100.

C. Research Support.

Ongoing Research Support

1) National Research Council from Argentina (CONICET): Associated Investigator in the grant: PIP 692, 2010-2012, title: "Regulation of hormonal sensitivity by activation of signaling pathways in the tumor microenvironment of mammary carcinomas", director Dr. Virgina Novaro.
2) Argentine National Agency for Scientific and Technical Promotion: "Adrenergic Receptors in human and experimental breast cancer". Grant PICT-2011-0103, 2012-2015.

Completed Research Support

1) Associated Investigator to PID N° 3-151200/88, CONICET ("Consejo Nacional de Investigaciones Científicas y Técnicas"): "Biochemical and molecular studies in normal and tumoral endocrine organs and cell lines", 1988-1991.
2) Alberto J. Roemmers Fundation: "Interaction between stress and hormone sensitive cancer", 1989-1990.
3) Alberto J. Roemmers Fundation: "Effect of stress on mammary tumors induced in rats by dimethylbenzanthracene", 1991-1992.
4) Associated Investigator to PID 252-0518-91. BID-CONICET: "Endocrinology and cell regulation ". Project: "Biochemical and molecular studies in normal and tumoral endocrine organs and cell lines", 1991-1994.
5) Alberto J. Roemmers Fundation: "Effect of α-adrenergic agonists and antagonists on tumors induced in rats by dimethylbenzanthracene", 1993-1994.
6) Alberto J. Roemmers Fundation: "α_2-adrenergic compounds in M3 mouse mammary tumors and MCF-7 human cell line. Effect of agonists y antagonists and description of α_2-adrenergic receptors in these tumors", 1996-1998.
7) Alberto J. Roemmers Fundation: "Biochemical and molecular studies in human breast diseases", 1999-2001.
8) Argentine CONICET: "Description and characterization of α_2-adrenergic receptors in human breast cancer cells", PIP 690, 1999-2003, Director.
9) Argentine National Agency for Scientific and Technical Promotion: "Biochemical and molecular studies in human breast diseases", 2002-2005.
10) Argentine CONICET: Co-director of the Research Project PIP 2004: 5351. Title: "Interaction between breast cancer cells and the cancer microenvironment and the bone marrow", 2005-2009.
11) Argentine National Agency for Scientific and Technical Promotion: "Biochemical and molecular studies in breast cancer ". Grant PICT 2004: 05-26046, 2006-2008.

12) Argentine director of the project *"*Alpha2-adrenergic receptors and proliferation of human breast cancer cells*"* Scientific and Technological Cooperation Program between the Argentine Ministry of Science, Technology and Productive Innovation from Argentine (Mincyt) and ECOS from France: 2008-2010.

Formation of Human Resources:

Direction of fellowships:

1) Verónica Wendel. Initiation Fellowship "Julio Poliacoff" granted by Bunge & Born, administered by the "Liga Argentina de Lucha Contra el Cáncer" (Argentine league for fighting cancer). Subject: "Effect of isolation stress on mammary tumors inducided in rats by dimethyl-benzanthracene. Its relation to α- y β- adrenergic compounds", 3-1-94 al 2-28-95.
2) Stella Maris Vázquez: Initiation Fellowship from CEDIQUIFA (Center for Studies of the Development of Chemical-Pharmaceutical Industry in Argentina). Subject: "Development of an assay to evaluate chemotherapy in human breast cancer samples from patients by primary culture", (July - Dec 1996).; Fellowship from the National Research Council from Argentina. Subject: "Description and characterization of α_2-adrenérgic receptors in human breast cancer cells". (Initiation: Oct 1997-Sept 1999); Perfecting: Oct 1999-Sept 2002).
3) Ariana Bruzzone: Doctoral Fellowship (CONICET). "α_2-adrenoceptors in experimental models of breast cancer" (2003-2007). Postdoctoral Fellowship (2009-2011).
4) Lilian Castillo: Doctoral Fellowship from the Argentine National Agency for Scientific and Technical Promotion (2005). Doctoral Fellowship from CONICET. Subject: "Interactions between α_2-adrenoceptors and lactogenic receptors in human breast cancer cells (2006-2010).
5) Cecilia Pérez Piñero: Doctoral Fellowship from CONICET. Subject: "Interactions of α_2-adrenoceptors in cancer and microenvironmental cells in human breast cancer" (2006-2010).

Direction of Thesis:

Degree:

1) Verónica Wendel. Subject: "Effect of isolation stress on mammary tumors induced in rats by dimethyl-benzanthracene. Its relation to α- y ß- adrenergic compounds". Presented on 2-2-28-94. Suma cum laude.
2) Ignacio Chiesa. Subject: "Contribution of α_2-adrenoceptors to the mitogenic effect of catecholestrogens in the breast cancer cell line MCF-7". Presented on 12-22-2004. Suma cum laude.
3) Cecilia Pérez. Subject: "Caracterization of adrenoceptors in human breast cancer cell lines". Presented on 3-27-2006. Suma cum laude.

Ph.D. degree:

1) Stella Maris Vázquez: "Description, characterization and regulation of α_2-adrenérgic receptors in human tumor and non-tumor breast cell lines". Dpt. of Biological Sciences, Exact and Natural Sciences School, University of Buenos Aires. Presented on 11-28-2001. Suma cum laude.
2) Co-director Pablo J. Enriori: "Estrogen and factors related to cell proliferation in human breast cysts". Pharmacy and Biochemistry School, University of Buenos Aires. Presented on 12-10-2002. Suma cum laude.
3) Ariana Bruzzone: "α_2-adrenergic action in breast cancer models". Pharmacy and Biochemistry, University of Buenos Aires. Presented on 09-02-2008. Suma cum laude.
4) Cecilia Pérez Piñero: "Effect of alfa2 and beta-adrenergic compounds in experimental models of human breast cancer". Exact and Natural Sciences School, University of Buenos Aires. Presented on 03-29-2011. Suma cum laude.

5) Lilian Castillo: “Interaction between α_2-adrenergic and prolactin receptor in human breast de cancer cells”. Pharmacy and Biochemistry School, University of Buenos Aires. Presented on 12-20-2012. Suma cum laude.