



Israel Roisenberg (1934-2013) – A life dedicated to science



Life History

Historians of science have continuously searched for the factors which determine why certain persons achieve prominence in the area. Of prime importance, of course, is their biological constitution; only persons with a given degree of intelligence can reach success. But there are many additional factors which are also important, including work drive, persistence, as well as appropriate family and academic environments.

This combination of factors led to Israel Roisenberg's brilliant career, and the main events of his life are listed in Table 1. He was born in Porto Alegre on July 31, 1934, where he lived all his life, except for varied periods of time in São Paulo and outside Brazil. After primary and secondary education (the latter in a public school, Colégio Júlio de Castilhos), he was approved in the Federal University of Rio Grande do Sul (UFRGS) entrance exam for the Biological Sciences Career in 1958. Soon he developed an interest in research, and as a consequence I invited him to work as an undergraduate student in our laboratory. He graduated in 1961 and soon afterwards received a contract as a Biologist at UFRGS. Our Post-Graduate Program was just starting at the time, but he also immediately enrolled as a Ph.D. student.

At the time I had just returned from the US, where I was enjoying a Post-Doctorate stay at the Department of Human Genetics, School of Medicine, University of Michigan in 1957/58, and was starting a research program in the area which involved not only the population genetics of Amerindians, but also medical genetics, due to the absence of specialists, at the time, in this field. Several hemophilia patients had looked for help in our Genetic Counseling Service, and therefore I suggested to Israel to work with this condition for his Doctoral Thesis.

This was the beginning of a distinguished interest in coagulation and hemostatic disorders that lasted for all his life. To learn the specific coagulation techniques he stayed for some time at the Butantan Institute in São Paulo, under the guidance of Gastão Rosenfeld, with whom he afterwards developed a strong friendship. The Ph.D. degree was awarded in 1968, and he was the first student to obtain it in our Program.

Newton E. Morton was at the time working in an extensive program of research with northeastern Brazilians, and one of the logical choices was that Israel would go to his laboratory for a Post-Doctorate stay. This occurred in 1968/69, and there he obtained skills in the electronic programs developed by Morton and performed field work in the Pacific Islands. As a result, they published papers summarizing the genealogical data obtained in the Pingelap and Mokil atolls (no. 5, List of Selected Publications) and the results of his Ph.D. Thesis (6). They also examined aspects of the population structure of Central and South American Amerindians (4).

Back in Brazil, he organized a highly successful group of research in hemostasis and was actively engaged in undergraduate and graduate teaching. In relation to the latter, 23 M.Sc. and 7 Ph.D. degrees were obtained under his guidance from 1974 up to 2005.

Along the years he made additional stays in the USA (1977) and Wales (1989), was the Coordinator of our Post-Graduate Program in Genetics and Molecular Biology for an extended period of time (1976-1992), President of the UFRGS Central Administration Post-Graduate Special Chamber (1991/96), and received national recognition as President of the Brazilian Society of Genetics (1974-1976), as Member of the Council, Brazilian Society for the Advancement of Science (SBPC) (1975/79), and was invited to join the Advisory Committees of the Brazilian National Council for Research and Development (CNPq) in 1985-1989 and 2000/2001, as well as to the Rio Grande do Sul State Foundation for the Development of Science (FAPERGS), from 1998 to 2001.

In 2006 he received the maximal reward a member of our community can achieve, Full Membership in the Brazilian Academy of Sciences; but unfortunately, soon afterwards, he suffered an extensive cerebral hemorrhagic accident which led to a state of coma that persisted until his death on November 5, 2013.

Research

During his academic career, Israel investigated a series of pathological conditions and was also interested in the development of new laboratory techniques. Details are given in the Selected List of his publications, below, which can be summarized as follows: (a) Hemophilias A and B (numbers 2, 6, 9, 11, 13, 16, 19, 20, 44); (b) Von Willebrand Factor and Disease, Factor V Deficiency (numbers 10, 12, 14, 21-23, 25-27, 30, 31); (c) Thrombophilia and other coagulation problems (numbers 7, 8, 39); (d) Diabetes (numbers 24, 29, 32-38, 40-43); (e) Other miscellaneous diseases: spherocytosis, hereditary non-hemolytic conjugated hyperbilirubinemia, adult polycystic kidney disease (numbers 1, 3, 28); and (e) Production of monoclonal and preparation of heterologous antibodies against the von Willebrand Factor (numbers 15, 17).

Family life, Personality

Israel was a devoted husband and father. In the difficult field work performed in the interior of Rio Grande do Sul for his Doctoral Thesis, searching for demographic and genealogical hemophilia information, he had to travel along muddy roads. But before reaching back home he would stop for shining his shoes and buying a flower bouquet for his wife, Paulina! He also took very seriously his role as father and grandfather with Mauro, Paulo, Claudio and four grandchildren, and was very affectionate to the other members of his family, which included his brother Samuel, a medical doctor who prematurely died in 2011; his sister Lea, who emigrated to Israel to do Zionist work; and Ari, Professor at the Geology Institute of UFRGS. In the weekends he loved to prepare the Gaúcho style barbecue (churrasco) for the family meetings.

He also had good manual skills, and used this in a workshop at his home where he even manufactured a complicated machine which helped him in the laboratory coagulation tests. He was very proud of his Jewish heritage, and although he abhorred violence, he took part in patrolling groups searching for anti-semitic profane violators of Jewish buildings and cemeteries in the still of the night.

Israel had also a strong devotion for science and was orthodox in relation to these matters. For instance, when certain politicians started talking about citizenship science he would strongly disagree "Science is science, no need for adjectives" he once said to me.

Table 1 - Main events related to the life of Israel Roisenberg.

Year	Event
1934	Born in Porto Alegre, RS on July 31, the son of Leon (a commercial representative) and Sarah Roisenberg.
1961	Graduated in Biological Sciences at the Federal University of Rio Grande do Sul (UFRGS).
1968	Ph.D. in Genetics and Molecular Biology, also at UFRGS.
1968	One-year post-doctorate stay at the University of Hawaii, USA, under the mentorship of Newton E. Morton.
1969	Return to Brazil and admission at the Santa Casa School of Medicine, São Paulo, SP.
1971	Admittance at the Genetics Department, Biosciences Institute, Federal University of Rio Grande do Sul, Porto Alegre, RS, as Associate Professor.
1974/76	President, Brazilian Society of Genetics.
1975/79	Member of the Council, Brazilian Society for the Advancement of Science (SBPC).
1976/92	Coordinator, Post-Graduate Program in Genetics and Molecular Biology, UFRGS in three mandates.
1977	Post-Doctorate stay at the Scripps Clinic and Research Foundation, La Jolla, CA, USA and Farmington University, New Mexico, USA.
1985	Approved as Full Professor at UFRGS.
1985/89, 2000/01	Member of the Advising Committee, National Council for Research and Development (CNPq), Brazil.
1989	Post-Doctorate stay at the University of Wales, Cardiff.
1991/96	President, Post-Graduate Special Chamber, UFRGS.
1998/01	Member, Advisory Committee, Rio Grande do Sul State Foundation for the Development of Science (FAPERGS).
2006	Elected to the Brazilian Academy of Sciences.
2006	Suffered an extensive cerebral hemorrhagic accident which led to a state of coma.
2013	Died on November 5.

He had a very pleasant personality, with a gentle sense of humor, was very dedicated to undergraduate and graduate teaching, had a cordial relationship with colleagues, laboratory and administrative personnel, and was kind enough to coordinate a paper honoring me in 1996 (no. 18, Selected List of Publications). Israel will certainly be sorely missed.

Selected List of Publications

1. Roisenberg I, Palombini BC and Petersen N (1962) Simultaneous occurrence of spherocytosis and polydactyly in a Brazilian family. *Acta Genet Med Gemellol* 11:55-70.
2. Roisenberg I (1964) Hemophilia B in a pair of monozygotic Negro twins. *Acta Genet Med Gemellol* 13:240-252.
3. Lima JEP, Utz E and Roisenberg I (1966) Hereditary non-hemolytic conjugated hyperbilirubinemia without abnormal liver cell pigmentation. *Am J Med* 40:628-633.

4. Roisenberg I and Morton NE (1970) Population structure of blood groups in Central and South American Indians. *Am J Phys Anthropol* 32:373-376.
5. Morton NE, Roisenberg I, Lew R and Yee S (1971) Pingelap and Mokil atolls: genealogy. *Am J Hum Genet* 23:350-360.
6. Roisenberg I and Morton NE (1971) Genetic aspects of hemophilias A and B in Rio Grande do Sul, Brazil. *Hum Hered* 21:97-107.
7. Colonia VJ and Roisenberg I (1979) Investigation of associations between ABO blood groups and coagulation, fibrinolysis, total lipids, cholesterol, and tryglycerides. *Hum Genet* 48:221-230.
8. Robinson WM and Roisenberg I (1980) Venous thromboembolism and ABO blood groups in a Brazilian population. *Hum Genet* 55:129-131.
9. Levisky RB, Thomaz C, Roisenberg I, Ferrari N, Rogatko A and Frota-Pessoa O (1983) Evaluation techniques for detection of hemophilia A heterozygotes. *Rev Bras Genet* 6:327-335.
10. Fischer RR, Pereira WM and Roisenberg I (1985) Inherited Factor V deficiency. *Hum Hered* 34:226-230.
11. Alexandre COP and Roisenberg I (1985) A genetic and demographic study of hemophilia A in Brazil. *Hum Hered* 35:250-254.
12. Fischer RR, Giddings JC and Roisenberg I (1988) Hereditary combined deficiency of clotting Factors V and VIII with involvement of von Willebrand Factor. *Clin Lab Haematol* 10:55-62.
13. Quezada-Diaz JE, Roisenberg I and Fischer RR (1988) A study of VIIC and VIICAg in normals and hemophilia A patients in a Brazilian population. *Rev Bras Genet* 11:193-202.
14. Fischer RR, Lerner C, Bandinelli E, Fonseca ASK and Roisenberg I (1989) Inheritance and prevalence of von Willebrand's Disease severe form in a Brazilian population. *J Inher Metabol Dis* 12:293-301.
15. Meissner RV, Roisenberg I and Nardi NB (1992) Production of monoclonal antibodies specific to human von Willebrand Factor. *Braz J Genet* 15:935-944.
16. Bandinelli E, Araujo AG, Roisenberg I and Figueiredo MS (1996) New mutations in the Factor IX gene in hemophilia B patients. (In Hemophilia B Database of Point Mutations and Short Additions and Deletions. F. Gianelli). *Nucleic Acids Res* 24:103-118.
17. Fischer RR, Lucas EM, Pereira AM and Roisenberg I (1996) Preparation of a heterologous antiserum for the determination of von Willebrand Factor in human plasma. *Braz J Med Biol Res* 29:1641-1644.
18. Roisenberg I, Schüler L, Jacques SM, Mattevi MS, Beigelman B, Freire-Maia N, Frota-Pessoa O and Cordeiro AR (1996) Homenagem ao Professor Francisco Mauro Salzano. *Braz J Genet* 19(Encarte):1-8.
19. Medeiros MA, Nunes AC, Bandinelli E and Roisenberg I (1999) Molecular and biochemical diagnosis of heterozygotes for hemophilia A: advantages and restrictions. *Proc XX World Cong Pathol Lab Med*: 37-40.
20. Rieger A and Roisenberg I (1999) Prevalence of Factor VIII inhibitors in patients with hemophilia A in Brazil. *Thromb Haemost* 81:475-476.
21. Simon D, Bandinelli E and Roisenberg I (2000) von Willebrand factor gene polymorphisms in three Brazilian ethnic groups. *Hum Biol* 72:1055-1063.
22. Schwartzmann G, Damin DC and Roisenberg I (2001) Malignant disease and von Willebrand Factor. *Lancet Oncol* 2:716-717.
23. Röhsig LM, Damin DC, Stefani SD, Roisenberg I, Castro C Jr and Schwartzmann G (2001) von Willebrand factor antigen levels in plasma of patients with malignant breast disease. *Braz J Med Biol Res* 34:1125-1129.
24. Crispim D, Tschiedel B, Souto KEP and Roisenberg I (2002) Prevalences of three mitochondrial DNA mutations in type 2 diabetic patients from southern Brazil. *Clin Endocrinol* 57:141-144.
25. Simon D, Palatnik M and Roisenberg I (2002) Analysis of the -1185A/G von Willebrand Factor (VWF) gene polymorphism in two Brazilian ethnic groups and its effects on the plasma VWF levels. *Thromb Res* 105:519-522.
26. Damin DC, Rosito MA, Gus P, Roisenberg I, Bandinelli E and Schwartzmann G (2002) von Willebrand Factor in colorectal cancer. *Int J Colorect Dis* 17:42-45.
27. Simon D, Bandinelli E and Roisenberg I (2003) Polymorphism in the promoter region of von Willebrand Factor gene and von Willebrand Disease Type 1. *Genet Mol Biol* 26:397-401.
28. Nunes ACF, Roisenberg I, Picolli EC, Weber R, Satler F, Grasselli F, Wainber F, Bohn F and Barros EJJ (2003) Adult polycystic kidney disease in patients on hemodialysis in the south of Brazil. *Nephrol Dial Transpl* 18:2686-2687.
29. Santos KG, Tschiedel B, Schneider JR, Souto KEP and Roisenberg I (2003) Diabetic retinopathy in Euro-Brazilian type 2 diabetic patients: relationship with polymorphisms in the aldose reductase, the plasminogen activator inhibitor-1 and the methylenetetrahydrofolate reductase genes. *Diabetes Res Clin Pract* 61:133-136.
30. Simon D, Paludo CA, Ghislenki GC, Manfroi W and Roisenberg I (2003) Association studies between the -1185A/G von Willebrand Factor gene polymorphism and coronary artery disease. *Braz J Med Biol Res* 36:709-714.
31. Simon D and Roisenberg I (2004) Type 2N von Willebrand Disease mutations in Brazilian individuals. *Haemophilia* 10:473-476.
32. Santos KG, Canani LH, Gross JL, Tschiedel B, Souto KEP and Roisenberg I (2005) Relationship of p22phox C242T polymorphism with nephropathy in type 2 diabetic patients. *J Nephrol* 18:733-738.
33. Canani LH, Capp C, Ng DPK, Choo SGI, Maia AL, Nabinger GB, Santos K, Crispim D, Roisenberg I, Krolewski AS and Gross JL (2005) The fatty acid binding protein -2A54T polymorphism is associated with renal disease in patients with type 2 diabetes mellitus. *Diabetes* 54:3326-3330.
34. Crispim D, Canani LH, Gross JL, Carlessi RM, Tschiedel B, Souto KEP and Roisenberg I (2005) The G1888A variant in the mitochondrial 16S rRNA gene is possibly associated with type 2 diabetes in Caucasian-Brazilian patients from southern Brazil. *Diabetic Med* 22:1683-1689.
35. Santos KG, Canani LH, Gross JL, Tschiedel B, Souto KEP and Roisenberg I (2005) The -374A allele of the receptor for advanced glycation end products (RAGE) gene is associated with a decreased risk of ischemic heart disease in Afri-

- can-Brazilians with type 2 diabetes. *Mol Genet Metab* 85:149-156.
36. Canani LH, Costa LA, Crispim D, Santos KG, Roisenberg I, Lisbôa HRK, Tres GS, Maia AL and Gross JL (2005) The presence of allele D of angiotensin converting enzyme polymorphism is associated with diabetic nephropathy in patients with 10 years duration of type 2 diabetes. *Diabetic Med* 22:1167-1172.
 37. Santos KG, Tschiedel B, Schneider JR, Souto KEP and Roisenberg I (2005) Prevalence of retinopathy in Caucasian type 2 diabetic patients from the south of Brazil and relationship with clinical and metabolic factors. *Braz J Med Biol Res* 38:221-225.
 38. Santos KG, Canani LH, Gross JL, Tschiedel B, Souto KEP and Roisenberg I (2006) The catalase 262C/T promoter polymorphism and diabetic complications in Caucasians with type 2 diabetes. *Dis Markers* 22:355-359.
 39. Dalmaz CA, Santos KG, Botton MR, Tedoldi CL and Roisenberg I (2006) Relationship between polymorphisms in thrombophilic genes and preeclampsia in a Brazilian population. *Blood Cells Mol Dis* 37:107-110.
 40. Crispim D, Fagundes NJR, Canani LH, Gross JL, Tschiedel B and Roisenberg I (2006) Role of the mitochondrial m.16189TC variant in type 2 diabetes mellitus in southern Brazil. *Diabetes Res Clin Pract* 74:204-206.
 41. Crispim D, Canani LH, Gross JL, Tschiedel B, Souto KEP and Roisenberg I (2006) Familial history of diabetes in patients with type 2 diabetes mellitus from southern Brazil and the influence on the clinical characteristics of this disease. *Arq Bras Endocrinol Metabol* 50:862-868.
 42. Santos KG, Canani LH, Gross JL, Tschiedel B, Souto KEP and Roisenberg I (2006) The -106CC genotype of the aldose reductase gene is associated with an increased risk of proliferative diabetic retinopathy in Caucasian-Brazilians with type 2 diabetes. *Mol Genet Metab* 88:280-284.
 43. Moreira, DC, Canani LH, Gross JL, Tschiedel B, Souto KEP and Roisenberg I (2006) The european-specific mitochondrial cluster J/T could confer an increased risk of insulin-resistance and type 2 diabetes: an analysis of the m.4216T > C and m.4917A > G variants. *Ann Hum Genet* 70:488-495.
 44. Leiria LB, Roisenberg I, Salzano FM and Bandinelli E (2009) Introns 1 and 22 inversions and factor VIII inhibitors in patients with severe haemophilia A in southern Brazil. *Haemophilia* 15:309-313.

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