DR. SHAY BEN-SHACHAR

The Gilber Isreali Neurofibromatosis Center, The genetic Institute
Tel- Aviv Sourasky Medical Center
6 Weizmann St, Tel-Aviv, Israel
Tel: 972-3-6974704 • Fax: 972-3-6974555
• E-mail: shayb@tlvmc.gov.il

POSITION TYTLE

Senior physician, The Gilbert Israeli NF center, and the Genetic Institute, Tel Aviv Medical Center, Tel Aviv, Israel

BIOGRAPHICAL

Birthplace: Tel-Aviv, Israel

EDUCATION

1998 *M.D.*, Tel-Aviv University, Sackler Faculty of Medicine,

POSTGRADUATE TRAINING and Positions

1997-1998	*Internship*, Sourasky Medical Center
1998-2002	*Pediatric Residency*, Dana Children's Hospital, Sourasky Medical Center,
2002-2003	*Clinical Genetics Fellowship*, Sourasky Medical Center
2003-2008	*Clinical Genetics Fellowship*, Department of Molecular and Human Genetics, Baylor College of Medicine
2003-2008	*Postdoctoral* Fellowship, Department of Molecular and Human Genetics, Baylor College of Medicine
2008- 2013	Senior Physician, The Genetic Institute and The Neurofibromatosis center, Tel-Aviv Sourasky Medical Center
2014-	Director-Pediatric Genetic Service, Sourasky Medical Center

LICENSURE

1998	*Medical License*, Israel Ministry of Health
2002	*Specialty in Pediatrics*, Israel Ministry of Health
2008	*Texas Faculty Medical Temporary License*
2008	*Specialty in Clinical Genetics*, Israel Ministry of Health

CERTIFICATIONS

2007 *Board Certified,* American Board of Medical Genetics

PROFESSIONAL SOCIETIES

American Society of Human Genetics
Isreali Society of Human Genetics
Israeli Genetic association-Secretary (2015-)

PUBLICATIONS

1. Lubetzky, R., Ben-Shachar, S, F. B. Mimouni, S. Dolberg. 2000. Mode of deliveri and neonatal hematocrit. *Am J Perinatol* 17:163-5.
2. **Ben-Shachar, S**., Z. Ou, C. Shaw, J. Belmont, M. S. Patel, M. Hummel, S. Amato, N. Tartaglia, J. Berg, V. R. Sutton, S. R. Lalani, A. C. Chinault, S. W. Cheung, J. R. Lupski, and A. Patel. 2008. 22q11.2 distal deletion: A novel recurrent genomic disorder distinct from DiGeorge syndrome/ Velocardiofacial syndrome. *Am J Hum Genet* 82: 217-21.
3. Fyffe, S., J. L. Neul, R. C. Samaco, T- H. Chao, **S. Ben-Shachar**, P. Moretti, B. E. McGill, E. H. Goulding, E. Sullivan, L. H. Tecott, H. Y. Zoghbi. 2008. Deletion of Mecp2 in Sim1-expressing neurons reveals a critical role for MeCP2 in feeding behavior, aggression, and the response to stress. *Neuron*, 59:947-58.
4. **Ben-Shachar, S**., M. Khajavi, M. A. Withers, C. A. Shaw, H. van Bokhoven, H. G. Brunner, and J. R. Lupski. 2009. Dominant versus recessive traits conveyed by allelic mutations - to what extent is nonsense mediated decay involved? *Clinical Genetics*, 75(4):394-400.
5. **Ben-Shachar, S**., L. Potocki, and S. R. Lalani. 2009. Severe hypotonia and SMA in an infant with an unbalanced chromosomal complement. *Am J Med Genet A* 149A(3):515-8.
6. **Ben-Shachar, S**., B. Lanpher, J. R. German, L. Potocki, S. C. Sreenath Nagamani, L. M. Franco, A. Malphrus, G. W. Bottenfield, J. E. Spence, S. Amato, B. Moghaddam, C. Skinner, S. A. Skinner, M. Shinawi,, A. Patel, S-W. Cheung, J. R. Lupski, A. L. Beaudet, and T. Sahoo. 2009. Microdeletion 15q13: A locus for autism, mental retardation, and psychiatric disorders with incomplete penetrance. *J Med Genet*, 46(6):382-8.
7. **Ben-Shachar, S.**, M. Chahrour, C. Thaller, C. A. Shaw, H. Y. Zoghbi. 2009. Mouse models of MeCP2 disorders share gene expression changes in the cerebellum and hypothalamus.
8. A. Erez, J. Li, M.T. Geraphty, **Ben-Shachar, S**, M.L.Cooper, D.E. Mensing, K.D.Vonalt, A.N. Pursley, A. Patel, S.W. Cheung, T. Sahoo, Mosaic deletion 11p13 in a child with dopamine beta-hydroxylase deficiency-case report and review of the literature. *Am J Med Genet A* 2010; 152A:732-6.
9. **Ben-Shachar, S**, A. Orr-Urtreger, E. Bardugo, R Shomrat, Y. Yaron Y. 2Large-scale population screening for spinal muscular atrophy: clinical implications. *Genet Med* 2010; 13:110-14.
10. Harris RA, Ferrari F, **Ben-Shachar, S**, Wang X, Saade G, Van Den Veyver I, Facchinetti F, Aagaard-Tillery K. Genome-wide array-based copy number profiling in human placentas from unexplained stillbirths. *Prenat Diagn* 2010; 31:932-44.

11. **Ben-Shachar S**, Zvi T, Rolfs A, Breda Klobus A, Yaron Y, Bar-Shira A, Orr-Urtreger A. A founder mutation causing a severe methylenetetrahydrofolate reductase (MTHFR). deficiency in Bukharian Jews. *Mol Genet Metab* 2012; 107(3):608-10.
12. Markus-Bustani K, Yaron Y, Goldstein M, Orr-Urtreger A, **Ben-Shachar S**. Undetected sex chromosome aneuploidy by chromosomal microarray. Prenat Diagn 2012 32(11):1117-8.
13. **Ben-Shachar S**, Constantini S, Hallevi H, Sach EK, Upadhyaya M, Evans GD, Huson SM. Increased rate of missense/in-frame mutations in individuals with NF1-related pulmonary stenosis: a novel genotype-phenotype correlation. *Eur J Hum Genet* 2012; 21:535-9.
14. Ben-Itzchak E, **Ben-Shachar S**, Zachor DA. Specific neurological phenotypes in autism spectrum disorders are associated with sex representation. *Aut research* 2013; 6:596-604.
15. Kim S, Chahrour M, **Ben-Shachar S**, Lim J. Ube3a/E6AP is involved in a subset of MeCP2 functions. *Biochem Biophys Res Commun* 2013; 437(1):67-73.
16. **Ben-Shachar S**, Yanai H, Baram L, Elad H, Meirovithz H, Ofer A, Brazowski E, Tulchinsky H, Pasmanik-Chor M, Dotan I. Gene expression profiles of ileal inflammatory bowel disease correlate with disease phenotype and advance understanding of its immunopathogenesis. *Inflamm Bowel Dis* 2013; 19:2509-21.
17. Zachor D.A, **Ben-Shachar S** &. Ben-Itzchak E. Do risk factors for autism spectrum disorders affect gender representation? *Res Autism Spectr Disord* 2013; 7:1397-1402.
18. Adler A, Topaz G, Heller K, Zeltser D, Ohayon T, Rozovski U, Halkin A, Rosso R, **Ben-Shachar S**, Antzelevitch C, Viskin S. Fever-induced Brugada pattern: How common is it and what does it mean? *Heart Rhythm* 2013; 10(9):1375-82.
19. Zachor DA, **Ben-Shachar S**, Curatolo P, et al. Recommendations for early diagnosis and intervention in Autism Spectrum Disorders: An Italian-Israeli Consensus Conference. *Eur J Ped Neurol* 2013; 18:107-118
20. Ayalon I, **Ben-Shachar S**, Eyal O, Weintrob N. Non-Classical 21-Hydroxylase Deficiency. *Hareffuah* (Hebrew) 2014; 6.
21. Bleyer AJ, Kmoch S, Antignac, Robins V, Kidd K, Kelsoe JR, Hladik G, Klemmer P, Knohl S, Scheinman SJ, Vo N, Santi A, Harris A, Canaday O, Weller N, Hulick PJ, Kristen Vogel K, Rahbari-Oskoui FF, Tuazon J, Deltas C, Somers D, Megarbane A, Kimmel PL, Sperati CJ, Orr-Urtreger A, **Ben-Shachar S**, Waugh DA, McGinn S, Bleyer, AJJ, Hodaňová K, Vyleťal P, Živná M, Hart TC, Hart PS. Variable Clinical Presentation of a *MUC1* Mutation Causing Medullary Cystic Kidney Disease Type 1. *CJASN* 2014; 9:527-35.
22. Bakry D, Aronson M, Durno C, Rimawi H, Farah R, Alharbi QK, Alharbi M, Shamvil A, **Ben-Shachar S**, Mistry M, Constantini1 S, Dvir R, Qaddoumi I, Ramyar L, Gallinger S, Lerner- Ellise J, Pollet A, Stephens D, Keiles S, Chao E, Malkin D, Bouffet E, Hawkins1 C, Tabori U. Novel genetic and clinical determinants of Constitutional Mismatch Repair Deficiency syndrome: Report from the CMMRD consortium. *Eur J Cancer* 2014; 50:987-96.
23. Feng L, **Ben-Shachar S**, Drori V, Orr-Uertreger A, Lupski j. Mechanism, Prevalence, and More Severe Neuropathy Phenotype of The Charcot-Marie-Tooth Type 1A Triplication. *Am J Hum Genet* 2014; 94:462-9.
24. Sukenik-Halevy R, Reches A, Bar-Shira A, Goldstein M, Orr-Ortreger A, Yaron Y, **Ben-Shachar S**. Microscopic chromosome Xp distal deletions - A challenging issue in prenatal genetic counseling. *Prenat Diagn* 2014; 34:592-7.
25. Weiss K, Orr-Urtreger A, Kaplan Ber I, Neiman T, Shomrat R, Bardugu E, Yaron, Y, **Ben-Shachar S**. Ethnic effect on FMR1 carrier rate and AGG repeats interruptions among Ashkenazi females. Genet Med 2014; 16:940-4.

26. **Ben-Shachar S***, Yanai H, Baram L, Elad H, Gitstein G, Brazowski E, Tulchinsky H, Pasmanik-Chor M, Dotan I. Gene Expression Alterations in Ulcerative Colitis Patients after Restorative Proctocolectomy Extend to the Small Bowel Proximal to the pouch. *GUT* 2014;
    *(contributed equally to the work)
27. **Ben-Shachar S***, Ayalon I, Reznik-Wolf H, Tenenbaum-Rakover Y, Zuckerman-Levin N, Cohen O, Lifshitz A, Fraenkel M, Toledano Y, Roash V, Koren I, Modan-Moses D, Hirsch D, Schachter-Davidov A, Israel S, Eyal O, Weintrob N. Androgen Receptor CAG Repeat Length in Relation to Phenotype Among Females with Non-Classical 21-Hydroxylase Deficiency**.** *Hormone and Metabolic Research* 2014;
    *(contributed equally to the work)
28. Bot G, Leshem D, Shiran SI, **Ben-Shachar S**, Constantini S, Roth J. Frontosphenoid synostosis: an unusual cause of anterior plagiocephaly. *J Craniofac Surg* 2015; 26:174-5.
29. Shlien A, Campbell B, de Borja R, Alexandrov L, Merico D, Wedge D, Van Loo P, Tarpey P, Coupland P, Behjati S, Pollett A, Meier B, Gerstung M, Merino D, Ramakrishna M, Remke M, Hodel KP, Henninger EE, Goksenin AY, Pearson C, Bakry D, Charames G, Druker H, Lerner-Ellis J, Mistry M, Dvir R, Arnold R, Grant R, Elchasid R, Farah R, Alexander S, **Ben Shachar S**, Ling SC, Gallinger S, Constantini S, Dirks P, Huang A, Scherer SW, Grundy RG, Meyn MS, Taylor MD, Durno C, Aronson M, Gartner A, Pursell ZF, Malkin D, Futreal PA, Stratton MR, Bouffet E, Hawkins C, Campbell PJ, Tabori U. Combined constitutional and somatic ablation of replication error repair results in massive mutation load and rapid cancer initiation. *Nat Genet* 2015; 47(3):257-62
30. Gan-Or Z, Alcalay RN, Bar-Shira A, Leblond CS, Postuma RB, **Ben-Shachar S**, Waters C, Johnson A, Levy O, Mirelman A, Gana-Weisz M, Dupré N, Montplaisir J, Giladi N, Fahn S, Xiong L, Dion PA, Orr-Urtreger A, Rouleau GA. Genetic markers of Restless Legs Syndrome in Parkinson disease. *Parkinsonism Relat Disord*. *In press*
31. Reinstein E, Smirin-Yosef P, Lagovsky I, Davidov B, Peretz Amit G, Neumann D, Orr-Urtreger A,**Ben-Shachar S**, Basel-Vanagaite L. A founder mutation in ADAMTSL4 causes early-onset bilateral ectopia lentis among Jews of Bukharian origin. Mol Genet Metab. 2015 Nov 26.
32. Edvardson S, Kose S, Jalas C, Fattal-Valevski A, Watanabe A, Ogawa Y, Mamada H, Fedick AM,**Ben-Shachar S**, Treff NR, Shaag A, Bale S, Gärtner J, Imamoto N, Elpeleg O. Leukoencephalopathy and early death associated with an Ashkenazi-Jewish founder mutation in the Hikeshi gene. J Med Genet. 2015
33. Dubov T, Toledano-Alhadef H, Chernin G, Constantini S, Cleper R, **Ben-Shachar S**. High prevalence of elevated blood pressure among children with neurofibromatosis type 1. Pediatr Nephrol. 2016 Jan;31(1):131-6.
34. Rojnueangnit K, Xie J, Gomes A, Sharp A, Callens T, Chen Y, Liu Y, Cochran M, Abbott MA, Atkin J, Babovic-Vuksanovic D, Barnett CP, Crenshaw M, Bartholomew DW, Basel L, Bellus G, **Ben-Shachar S**, Bialer MG, Bick D, Blumberg B, Cortes F, David KL, Destree A, Duat-Rodriguez A, Earl D, Escobar L, Eswara M, Ezquieta B, Frayling IM, Frydman M, Gardner K, Gripp KW, Hernández-Chico C, Heyrman K, Ibrahim J, Janssens S, Keena BA, Llano-Rivas I, Leppig K, McDonald M, Misra VK, Mulbury J, Narayanan V, Orenstein N, Galvin-Parton P, Pedro H, Pivnick EK, Powell CM, Randolph L, Raskin S, Rosell J, Rubin K, Seashore M, Schaaf CP, Scheuerle A, Schultz M, Schorry E, Schnur R, Siqveland E, Tkachuk A, Tonsgard J, Upadhyaya M, Verma IC, Wallace S, Williams C, Zackai E, Zonana J, Lazaro C, Claes K, Korf B, Martin Y, Legius E, Messiaen L. High Incidence of Noonan Syndrome Features Including Short Stature and Pulmonic Stenosis in Patients carrying NF1 Missense Mutations Affecting p.Arg1809: Genotype-Phenotype Correlation. Hum Mutat. 2015 Nov;36(11):1052-63.

35. Sukenik-Halevy R, Ludman MD, **Ben-Shachar S**, Raas-Rothschild A. The time-consuming demands of the practice of medical genetics in the era of advanced genomic testing. Genet Med. 2015

36. Elhasid R, Dvir R, Rosenfeld Keidar H, Ben Shachar S, Bitan M, Solar I, Durno C, Aronson M, Malkin D, Hawkins C, Bouffet E, Tabori U; BMMRD Consortium. Management of Acute Myeloblastic Leukemia in a Child With Biallelic Mismatch Repair Deficiency. J Pediatr Hematol Oncol. 2015 Nov;37(8):e490-3
37. Mashiah J, Harel A, Bitterman O, Sagi L, Gat A, Fellig Y, **Ben-Shachar S**, Sprecher E. sotretinoin treatment of autosomal recessive congenital ichthyosis complicated by coexisting dysferlinopathy.. Clin Exp Dermatol. 2016 Jun;41(4):390-3
38. Shofty B, Constantini S, **Ben-Shachar S**. Advances in Molecular Diagnosis of Neurofibromatosis Type 1. Semin Pediatr Neurol. 2015 Dec;22(4):234-9.
39. Dubov T, Toledano-Alhadef H, Bokstein F, Constantini S, **Ben-Shachar S**. The effect of parental age on the presence of de novo mutations - Lessons from neurofibromatosis type I. Mol Genet Genomic Med. 2016 Jun 16;4(4):480-6
40. **Ben-Shachar S**, Yanai H, Sherman Horev H, Elad H, Baram L, Issakov O, Tulchinsky H, Pasmanik-Chor M, Shomron N, Dotan I. MicroRNAs Expression in the Ileal Pouch of Patients with Ulcerative Colitis Is Robustly Up-Regulated and Correlates with Disease Phenotypes. PLoS One. 2016 Aug 18;11(8)
41. Fox J, **Ben-Shachar S**, Uliel S, Svirsky R, Saitsu H, Matsumoto N, Fattal-Valevski A. Rare familial TSC2 gene mutation associated with atypical phenotype presentation of Tuberous Sclerosis Complex. Am J Med Genet A. 2017 Mar;173(3):744-748.
42. **Ben-Shachar S**, Dubov T, Toledano-Alhadef H, Mashiah J, Sprecher E, Constantini S, Leshno M, Messiaen LM. Predicting neurofibromatosis type 1 risk among children with isolated café-au-lait macules. J Am Acad Dermatol. 2017 Jun;76(6):1077-1083.
43. Bokstein F, Dubov T, Toledano-Alhadef H, Bernstein-Molho R, Constantini S, Evans DG, **Ben-Shachar S**. Cranial irradiation in childhood mimicking neurofibromatosis type II. Am J Med Genet A. 2017 Jun;173(6):1635-1639
44. Yanai H, **Ben-Shachar S**, Mlynarsky L, Godny L, Leshno M, Tulchinsky H, Dotan I. The outcome of ulcerative colitis patients undergoing pouch surgery is determined by pre-surgical factors. Aliment Pharmacol Ther. 2017 Sep;46(5):508-515
45. Biancalana V, Scheidecker S, Miguet M, Laquerrière A, Romero NB, Stojkovic T, Abath Neto O, Mercier S, Voermans N, Tanner L, Rogers C, Ollagnon-Roman E, Roper H, Boutte C, **Ben-Shachar S**, Lornage X, Vasli N, Schaefer E, Laforet P, Pouget J, Moerman A, Pasquier L, Marcorelle P, Magot A, Küsters B, Streichenberger N, Tranchant C, Dondaine N, Schneider R, Gasnier C, Calmels N, Kremer V, Nguyen K, Perrier J, Kamsteeg EJ, Carlier P, Carlier RY, Thompson J, Boland A, Deleuze JF, Fardeau M, Zanoteli E, Eymard B, Laporte J. Affected female carriers of MTM1 mutations display a wide spectrum of clinical and pathological involvement: delineating diagnostic clues. Acta Neuropathol. 2017 Dec;134(6):889-904
46. Isakov O, Dotan I, **Ben-Shachar S**. Machine Learning-Based Gene Prioritization Identifies Novel Candidate Risk Genes for Inflammatory Bowel Disease. Inflamm Bowel Dis. 2017 Sep;23(9):1516-1523
47. Mauda-Havakuk M, Shofty B, **Ben-Shachar S**, Ben-Sira L, Constantini S, Bokstein F. Spinal and Paraspinal Plexiform Neurofibromas in Patients with Neurofibromatosis Type 1: A Novel Scoring System for Radiological-Clinical Correlation. AJNR Am J Neuroradiol. 2017 Oct;38(10):1869-1875

48. **Ben-Shachar S**, Afawi Z, Masalha R, Badarny S, Neiman T, Pavzner D, Bar-Shira A, Orr-Urtreger A. Variable PARK2 Mutations Cause Early-Onset Parkinson's Disease in a Small Restricted Population. J Mol Neurosci. 2017 Oct;63(2):216-222
49. Koczkowska M, Chen Y, Callens T, Gomes A, Sharp A, Johnson S, Hsiao MC, Chen Z, Balasubramanian M, Barnett CP, Becker TA, **Ben-Shachar S**, Bertola DR, Blakeley JO, Burkitt-Wright EMM, Callaway A, Crenshaw M, Cunha KS, Cunningham M, D'Agostino MD, Dahan K, De Luca A, Destrée A, Dhamija R, Eoli M, Evans DGR, Galvin-Parton P, George-Abraham JK, Gripp KW, Guevara-Campos J, Hanchard NA, Hernández-Chico C, Immken L, Janssens S, Jones KJ, Keena BA, Kochhar A, Liebelt J, Martir-Negron A, Mahoney MJ, Maystadt I, McDougall C, McEntagart M, Mendelsohn N, Miller DT, Mortier G, Morton J, Pappas J, Plotkin SR, Pond D, Rosenbaum K, Rubin K, Russell L, Rutledge LS, Saletti V, Schonberg R, Schreiber A, Seidel M, Siqveland E, Stockton DW, Trevisson E, Ullrich NJ, Upadhyaya M, van Minkelen R, Verhelst H, Wallace MR, Yap YS, Zackai E, Zonana J, Zurcher V, Claes K, Martin Y, Korf BR, Legius E, Messiaen LM. Genotype-Phenotype Correlation in NF1: Evidence for a More Severe Phenotype Associated with Missense Mutations Affecting NF1 Codons 844-848. Am J Hum Genet. 2018 Jan 4;102(1):69-87
50. Sagi-Dain L, Maya I, Peleg A, Reches A, Banne E, Baris HN, Tenne T, Singer A, **Ben-Shachar S**. Microarray analysis in pregnancies with isolated unilateral kidney agenesis. Pediatr Res. 2018 Apr;83(4):825-828
51. Sagi-Dain L, Maya I, Falik-Zaccai T, Feingold-Zadok M, Lev D, Yonath H, Kaliner E, Frumkin A, **Ben Shachar S**, Singer A. Isolated fetal horseshoe kidney does not seem to increase the risk for abnormal chromosomal microarray results. Eur J Obstet Gynecol Reprod Biol. 2018 Mar;222:80-83

    Maya I, Singer A, Baris HN, Goldberg Y, Shalata A, Khayat M, **Ben-Shachar S**, Sagi-Dain L. Prenatal microarray analysis in right aortic arch-a retrospective cohort study and review of the literature. J Perinatol. 2018 May;38(5):468-473
52. Sagi-Dain L, Singer A, Hadid Y, Sharony R, Vinkler C, Bar-Shira A, Segel R, **Ben Shachar S**, Maya I. Non-visualization of fetal gallbladder in microarray era - a retrospective cohort study and review of the literature. J Matern Fetal Neonatal Med. 2018 Feb 28:1-6
53. Singer A, Maya I, Koifman A, Nasser Samra N, Baris HN, Falik-Zaccai T, **Ben Shachar S**, Sagi-Dain L. Microarray analysis in pregnancies with isolated echogenic bowel. Early Hum Dev. 2018 Apr;119:25-28
54. Weintrob N, Eyal O, Slakman M, Segev Becker A, Israeli G, Kalter-Leibovici O, **Ben-Shachar S**. The effect of CAG repeats length on differences in hirsutism among healthy Israeli women of different ethnicities. PLoS One. 2018 Mar 27;13(3)
55. Sherman Horev H, Rabinowitz KM, Elad H, Barkan R, **Ben-Shachar S**, Pasmanik Chor M, Dotan I. Increase in Processing Factors Is Involved in Skewed MicroRNA Expression in Patients with Ulcerative Colitis Who Develop Small Intestine Inflammation after Pouch Surgery. Inflamm Bowel Dis. 2018 Apr 23;24(5
56. Magoulas PL, Shchelochkov OA, Bainbridge MN, **Ben-Shachar S**, Yatsenko S, Potocki L, Lewis RA, Searby C, Marcogliese AN, Elghetany MT, Zapata G, Hernández PP, Gadkari M, Einhaus D, Muzny DM, Gibbs RA, Bertuch AA, Scott DA, Corvera S, Franco LM. Syndromic congenital myelofibrosis associated with a loss-of-function variant in *RBSN*. Blood. 2018 Aug 9;132(6):658-662
57. Sagi-Dain L, Singer A, Frumkin A, Shalata A, Koifman A, Segel R, Benyamini L, Rienstein S, Kahyat M, Sharony R, Maya I, **Ben Shachar S**. Chromosomal microarray findings in pregnancies with an isolated pelvic kidney. J Perinat Med. 2018 May 29