



Frankie li
Stuyvesant H.S
May 28, 2013

MARFAN SYNDROME

Physiology

- 1 in 10,000 to 1 in 20,000 incidence
- Multi-system disorder, targets connective tissue
- Features worsen with age, not much shown at birth
- Autosomal Dominant
- Affected individuals have a multitude of disorders:
 - I. Skeletal abnormalities: Disproportionate tall stature, pectus deformities, scoliosis, joint laxity, arachnodactyly
 - II. Ocular abnormalities: displacing of lens, flat corneas, increased globe length, and hypoplastic irides
 - III. Cardiovascular abnormalities: Mitral valve prolapse, aortic regurgitation, aortic dilation, aortic dissection
 - IV. Skin abnormalities: striae atrophicae and recurrent herniae
 - V. Dural abnormalities: lumbosacral ectasia

*Possibility that Abraham Lincoln & Pharaoh Akhenaten was affected

Molecular Cause

- Mutation in the FBN1 gene on chromosome 15 (15q21.1)
- More than 1.000 FBN1 gene mutations cause Marfan Syndrome identified up-to-date
- There are mutations in FBN1 that don't cause Marfan
- Fibrillin-1 produced by FBN1 gene
- Molecular pathway:
 - Less microfibrils are formed → weak elastic fibers
 - Weak elastic fibers → Excess TGF- β proteins
 - Excess TGF- β proteins → elasticity in tissues decreased
 - Elasticity decreased → Overgrowth + Instability
 - Overgrowth + Instability → Marfan Syndrome
 - Overproduction of TGF- β proteins can cause cancer

Treatments/Risks and Limits

- Very difficult to diagnose
 - Mutations vary
 - Features develop with age
- No reliable prenatal test
- Diagnosis made through examination of patients eyes, heart, and bone structure
- Surgeries
 - Replacement of eye lens
 - Surgery for scoliosis
 - Chest-wall reconstruction
 - Replacement of aorta
- Management
 - Yearly MRI's
 - Yearly assessments
 - Physical therapy
 - Orthotic
 - Restriction of participation in strenuous activities
 - Beta-adrenergic blockers

Proposed Cure & Limits

- Stem cells
 - Used to increase the amount of micro fibrils
 - Research still being done
- Losarton
 - Angiotensin receptor blocker
 - Causes peripheral blood vessels to narrow
 - Stimulates production of aldosterone which causes salt and water to be retained by kidneys
 - Stimulates TGF- β proteins as well
 - Life-long usage required
 - Cannot be taken during pregnancy
- Collagen
 - Increase production
 - Strengthens elastic fibers

References

- "FBN1." - *Fibrillin 1*. N.p., Mar. 2012. Web. 08 May 2013. <<http://ghr.nlm.nih.gov/gene/FBN1>>
- "Genes and Mapped Phenotypes." *National Center for Biotechnology Information*. U.S. National Library of Medicine, 27 Apr. 2013. Web. 08 May 2013. <<http://www.ncbi.nlm.nih.gov/gene/25805>>.
- Huang, Audrey. "Drug Treatment for Marfan Syndrome Looks Promising." *Johns Hopkins Children's Center: Drug Treatment for Marfan Syndrome Looks Promising*. John Hopkins Children's Center, 3 July 2008. Web. 08 May 2013. <<http://www.hopkinschildrens.org/drug-treatment-marfan-syndrome.aspx>>.
- Milewicz, Dianna M. "Treatment of Aortic Disease in Patients With Marfan Syndrome." *Treatment of Aortic Disease in Patients With Marfan Syndrome*. American Health Association, n.d. Web. 08 May 2013. <<http://circ.ahajournals.org/content/111/11/e150.full>>.
- "New Player Identified in Cellular Relay Event That Suppresses Cancer." *DukeHealth.org*. Duke Medical News and Communications, 5 Sept. 2003. Web. 08 May 2013. <http://www.dukehealth.org/health_library/news/7134>.
- Nussbaum, Robert L., Roderick R. McInnes, Huntington F. Willard, Ada Hamosh, and Margaret W. Thompson. *Thompson & Thompson Genetics in Medicine*. Philadelphia: Saunders/Elsevier, 2007. Print.
- Summers, KM. "Result Filters." *National Center for Biotechnology Information*. U.S. National Library of Medicine, 24 Oct. 2009. Web. 08 May 2013. <<http://www.ncbi.nlm.nih.gov/pubmed/19573590>>.
- Waclawik, Gabrielle. "Fibrillin Pathway - FBN1 and Marfan Syndrome." *Fibrillin Pathway - FBN1 and Marfan Syndrome*. N.p., 13 May 2010. Web. 08 May 2013. <<http://waclawikgen677510.weebly.com/fibrillin-pathway.html>>.
- "What Is Collagen?" *WiseGEEK*. N.p., n.d. Web. 08 May 2013. <<http://www.wisegeek.org/what-is-collagen.htm>>.
- "Akhenaten (Amenhotep IV)." *Ancient Egypt Pharaohs*. N.p., n.d. Web. 19 May 2013. <<http://ancientegyptonline.co.uk/akhenaten.html>>.
- A., Biggin, Holman K., Brett M., Bennetts B., and Ades L. "Result Filters." *National Center for Biotechnology Information*. U.S. National Library of Medicine, 24 Jan. 2004. Web. 8 May 2013. <<http://www.ncbi.nlm.nih.gov/pubmed/14695540>>.
- Canadas, Victoria, Isidre Vilacosta, Isidora Bruna, and Valentin Fuster. "Marfan Syndrome. Part 1: Pathophysiology and Diagnosis." *Nature Reviews Cardiology* 10.3 (2010): 1-10. Web. 8 May 2013. <<http://www.sindromemarfan.cat/docs/rm1.pdf>>.
- "Losartan Questions and Answers." *National Marfan Foundation*. N.p., n.d. Web. 8 May 2013. <<http://www.marfan.org/marfan/2526/Losartan-Questions-and-Answers>>.
- *National Center for Biotechnology Information*. U.S. National Library of Medicine, 1 Apr. 2013. Web. 21 May 2013. <<http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0010993/?report=details>>.
- "Cozaar (losartan)." *Netdoctor*. Net Doctor, 2 May 2007. Web. 21 May 2013. <<http://www.netdoctor.co.uk/heart-and-blood/medicines/cozaar.html>>.
- Campbell, Scott E., and Laxmansa C. Katwa. "Angiotensin II Stimulated Expression of Transforming Growth Factor- β 1 in Cardiac Fibroblasts and Myofibroblasts." *Journal of Molecular and Cellular Cardiology* 29.7 (1997): 1947-958. Print.