VCFSEF Newsletter

Voice of the VCFS Educational Foundation **Winter 97 December 1, 1997**

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A Note From the President

It was with great pleasure that I accepted the Presidency of the Velo-Cardio-facial Syndrome Educational Foundation at the conference in Palo Alto this past May. It promises to be an exciting year and I hope to help further the cause of the Foundation during these coming months.

Our eight year old son, Eamon, was diagnosed as VCFS five years ago. My husband, Don, and I know firsthand the unique challenges that this represents. We also know that it is imperative to disseminate knowledge to the parents, educators and medical community involved with these children. This is the primary purpose of our working together as a Foundation. This year, the Foundation may reach 2,000 members. That number promises to grow over the next few years as we continue to educate others and help parents obtain the diagnosis they need to obtain medical and educational assistance for their children.

At each year's VCFS Educational Foundation meeting, I have had the pleasure of meeting many parents and medical professionals who are working diligently to help others cope with the difficulties of VCFS. At these meetings, I derive a sense of camaraderie from the parents and family members and hope from those who are searching for answers to the various manifestations of the disorder.

As coordinator of the Northeast VCFS Support Group, I am encouraged by the response, both from the medical community and the families who want to become involved. Our group is not yet a year old and we have almost 100 members on our roster. They all have one thing in common; to better the lives of those who have VCFS.

Our Northeast Group has also been working with parents from the United States and Canada who have expressed an interest in starting their own support groups. We have informally assembled a packet of information to help others begin the rewarding process of coordinating a support group. Please contact me if you would like this information.

One of my goals for the coming year is to compile a database of Foundation members to facilitate a network. This would, hopefully, allow members to interact with those in their immediate area who are facing similar challenges. At the first meeting of our Northeast Group we were amazed to find that many members lived in the same town. Some resided on adjacent streets and, prior to our meeting, had not known one another!

It is imperative that we keep our lines of communication open and work together to accomplish the tasks of the coming year. To this end, please do not hesitate to call, write or e-mail me at the following address. I look forward to hearing from you and seeing you at our next meeting.

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In this issue...

A Note From the Editor

Let me take this opportunity to introduce myself to those of you I did not meet at the conference in Palo Alto. I am a board-certified genetic counselor at Children's National Medical Center in Washington, D.C. I work primarily in pediatrics. My first exposure to children with VCFS was as a graduate student when I rotated through Dr. Shprintzen's clinic. In my present position, I have grown fond of the families we follow with VCFS and am in the process of organizing a multidisciplinary clinic for the disorder.

We delayed this issue to bring you summaries of some of the latest research presented at the American Society of Human Genetics annual meeting in Baltimore at the end of October. Also in this issue is a list and review of some recent publications. I will make this a regular feature of the Newsletter. At the request of several families we will list local support groups and contact people and add a Pen Pals Corner for children and families.

I am excited about being part of the VCFS Educational Foundation and hope people will write or e-mail me their comments and suggestions for future editions.

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Pen Pals

Anyone interested in having a pen pal should write to to the Editor's address or e-mail, stating your name, age, address, and anything else you want me to know (hobbies,

school, etc.). If you are a parent, tell me about your child. I will try to match you with another person with similar interests.

Local Support Groups

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Announcing the 4th Annual Meeting of the Velo-Cardio-Facial Syndrome Educational Foundation
Our 4th annual meeting will be held in Boston at the Harvard Medical School, June 26-28, 1998. Pre-registration forms, abstract forms, call for papers, call for suggestions, and meeting information will be mailed shortly. Partial funding is being provided by Children's Hospital of Boston and its Medical Staff. Plan on being there!!

1997 VCFS - Related Publications

Bonnet D, Cormier-Daire V, Kachaner J, Szezepanski I, Souillard P, Sidi D, Munnich A and Lyonnet S. Microsatellite DNA markers detects 95% of chromosome 22q11 deletions. American Journal of Medical Genetics 1997 Jan 20:68(2):182-184. *The article describes the use of microsatelitte DNA markers to detect 22q11 deletions in infants with a cono-truncal malformation. The test results are available within 24 hours.*

Carlson C, Sirotkin H, Pandita R, Goldberg R, McKie J, Wadey R, Patanjali SR, Weissman SM, Anyane-Yeboa K Warburton D, Scambler P, Shprintzen R, Kucherlapati R, and Morrow BE. Molecular definition of 22q11 deletions in 151 velo-cardio-facial syndrome patients. American Journal of Human Genetics 1997 Sept;61(3):620-629. *151 patients with VCFS were genotyped using 15 consecutive polymorphic markers in 22q11. No correlation between the presence or size of the deletion and the phenoytpe was found. A physical map of a 1,080 kb region was constructed and a 480 kb critical region for VCFS was delineated, including genes or GSCL, CTP, CLTD, HIRA and TMVCF as well as a number of novel ESTs.*

Carlson C, Papolos D, Pandita RK, Faedda GL, Veit S, Goldberg R, Shprintzen R, Kucherlapati R and Morrow B. Molecular analysis of Velo-Cardio-Facial Syndrome patients with psychiaric disorders. American Journal of Human Genetics 1997 60:851-859. *26 patients with VCFS were screened for psychiatric illness and deletions of the 22q11 region. Although there was no correlation between the phenotype of psychiatric illness and specific deletions, there was a high prevalence of bipolar spectrum disorders among the VCFS patients suggesting a common genetic etiology.*

Devriendt K, Van Hoestenberghe R, Van Hole C, Devlieger H, Gewillig M, Moerman P, Van den Berghe H and Fryns JP. Submicroscopic deletion in chromosome 22q11 in trizygous triplet siblings and their father. Clinical variability of 22q11 deletion. Clinical Genetics 1997 Apr;51(4):246-249. *A submicroscopic deletion was detected in triplets and their father. Two of the children has DiGeorge sequence, conotruncal heart disease, and hypoplastic thymus. The third child had features of both DiGeorge and VCFS while the father had features of VCFS. This family further illustrates the wide variability in expression of a deletion of 22q11, even within one family.*

Galili N, Baldwin HS, Lund J, Reeves R, Gong W, Wang Z, Roe BA, Emanuel BS, Nayak S, Mickanin C, Budarf ML and Buck CA. A region of mouse chromosome 16 is syntenic to the DiGeorge, velo-cardio-facial syndrome minimal critical region. Genomic Research 1997 Jan;7(1):17-26. *This article report on synteny between a 150 kb region on mouse chromosome 16 and the most commonly deleted region of 22q11. Comparative sequence analysis of a 38 kb segment reveals similarities in gene content, order, exon composition and transcription direction.*

Gong W, Emanuel BS, Galili N, Kim DH, Roe B, Driscoll DA and Budarf ML. Structural and mutational analysis of a conserved gene(DGSI) from the minimal DiGeorge syndrome critical region. Human Molecular Genetics 1997 Feb;6(2):267-276.

Goldmuntz E and Emanual BS. Genetic disorders of cardiac morphogenesis. The DiGeorge and velo-cardio-facial syndromes. Circulation Research 1997 Apr;80(4):437-443.

Holmes SE, Riazi MA, Gong W, McDermid HE, Sellinger BT, Hua A, Chen F, Wang Z, Xhang G, Roe B, Gonzalez I, McDonald-McGinn DM, Zackai E, Emanuel BS and Budarf ML. Disruption of the clathrin heavy chain-like gene (CLTCL) associated with features of DGS/VCFS: a balanced (21;22)(p12;q11) translocation. Human Molecular Genetics 197 Mar;6(3):357-367.

Hou JW, Wang JK, Tsai WY, Chou CC and Wang TR. CATCH 22: deletion of locus 22q11 in velo-cardio-facial syndrome, DiGeorge anomaly, and nonsyndromic conotruncal defects. Journal of the Formosa Medical Association 197 Jun;96(6):149-423.

Jaquez M, Driscoll DA, Li M, Emanuel BS, Hernandez I, Jaquez F, Lembert N, Ramirez J and Matalon R. Unbalanced 12;22 translocation in a patient with manifestation of DiGeorge and velo-cardio-facial syndrome. American Journal of Medical Genetics 1997 May 2;70(1):6-10. *A case report of a patient with an unbalanced 15;22 translocation. Her karyotype was 45, XX, der(15)t(15;22)(p11.2;q11.2), -22. FISH studies confirmed the loss of the proximal DiGeorge chromosomal region.*

Lachman HM, Kelsoe JR, Remick RA, Sadovnick AD, Rapaport MH, Lin M, Pazur BA, Roe AM, Saito T and Papolos, DF. Linkage studies suggest a possible focus for bipolar disorder near the velo-cardio-facial syndrome region on chromosome 22. American Journal of Medical Genetics 1997 Apr 18; 74(2):121-128. *17 families with bipolar disorder were studied using three microsatellite markers spanning 13 cM around the VCFS region. Linkage analysis suggest a possible locus for bipolar disorder near the VCFS region on chromosome 22.*

Marino B, Digilio MC, Novelli G, Giannotti A and Dallapiccola B. Tricuspid atresia and 22q11 deletion. American Journal of Medical Genetics 1997 Oct 3; 72(1):40-42. *Tricuspid atresia is not commonly included as a common heart defect associated with VCFS. 26 children withtricuspis atresia were screened for the deletion in 22q11. Two were found to have the deletion suggesting that tricuspid atresia should be associated with VCFS.*

Pizzut A, Novelli G, Ratti A, Amati F, Mari A, Calabrese G, Nicolis S, Simani V, Marino B, Scarlato G, Ottolenghi S and Dallapiccola B. UFD1L, a developmentally expressed ubiquitous gene, is deleted in CATCH 22 syndrome. Human Molecular Genetics 1997 Feb;6(2):259-265.

Sirotkin H, O'Donnell H, DasGupta R, Halford S, StJore B, Puech A, Parimoo S, Morrow B, Skoultchi A, Weissman SM, Scambler P and Kucherlapati R. Identification of a new human catenin gene family member (ARVCF) from the region deleted in velo-cardio-facial syndrome. Genomics 1997 Apr1;41(1):75-83.

Swillen A, Devriendt K, Legius E, Eyskens B, Dumoulin M, Gewillig M and Fryns JP. Inteligence and psychosocial adjustment in velocardiofacial syndrome: a study of 37 children and adolescents with VCFS. Journal of Medical Gentics 1997 Jun;34(6):453-458.

Thomas JA and Graham JM Jr. Chromosome 22q11 Deletion Syndrome: An Update and review for the primary pediatrician. Clinical Pediatrics May 1997; 35(5) 253-266. *The article summarizes the etiology, clinical findings (broken down system by system), the natural history and surveillance recommendations for the primary pediatrician.*

Worthington S, Colley A, Fagan K, Dai K and Lipson AH. Anal anomalies: an uncommon feature of velocardiofacial (Shprintzen) syndrome? Journal of Medical Genetics 1997 Jan;34(1):79-82.

Report on the 1997 Annual Meeting of the American Society of Human Genetics

Once again, the scientific program at the annual meeting of the American Society of Human Genetics had an abundance of presentations and poster sessions directly or indirectly involving velo-cardio-facial syndrome. Approximately 5,000 professionals from around the world attended the meeting in Baltimore from October 28-November 1, 1997. Papers on VCFS and related subjects came from the U.S., Canada, France, Great Britain, and Japan. Listed below are titles of the presentations, authors' names, the location of the first author, and the abstract number as listed in Volume 61 of the American Journal of Human Genetics (October issue, number 4). Brief summaries based on the presentations, posters, abstracts, or discussions with the author are provided. The papers are presented in the numerical order of their abstract numbers. Numbers over 2109 represent published abstracts which were not selected for presentation at the meeting:

The behavioural phenotype in velo-cardio-facial syndrome. K.C. Murphy, M.J. Owen, University of Wales, Cardiff, Wales, Abstract 15. *A psychiatric analysis of 40 patients with VCFS, 17 to 45 years of age is reported. 25% met diagnostic criteria for schizophrenia or schizoaffective disorder, 13% had major depression without psychosis, 3% had rapid cycling bipolar disorder.*

Vascular anomalies may explain many of the features of velo-cardio-facial syndrome. R.J. Shprintzen, B. Morrow, R. Kucherlapati, State University of New York Health Science Center at Syracuse, Syracuse, NY, Abstract 16. *The authors suggest that most of the anomalies in VCFS may actually be secondary malformations, caused by an interruption of normal development by vascular insufficiency or vascular disruption. As evidence, a wide range of vascular anomalies are presented based on the review of 371 cases. The authors state that the most common anomalies in VCFS are vascular, and they may explain the more than 170 anomalies previously reported in the syndrome, including many of the structural and behavioral abnormalities.*

A duplication on chromosome 22q11 is the basis for the common deletion that occurs in velo-cardio-facial syndrome patients. B.E. Morrow, L. Edelmann, J. Ferreira, R.K. Pandita, C.G. Carlson, J.E. Procter, M. Jackson, D. Wilson, R. Goldberg, R.J. Shprintzen, R. Kucherlapati, Abstract 25. *The authors report that the common breakpoints in VCFS occur within a region of duplicated sequences of DNA. The duplication was 40 kilobases in size. Intrachromosomal recombination or unequal crossing over resulting in the duplicated segments of DNA which provide the breakpoints for the most common deletion is hypothsized.*

Microdeletion 22q11.2: clinical data and deletion size. J. Siegel-Bartelt, B. Beatty, T. Scheid, K. Henderson, C. Cytrynbaum, G. Nier, B.S. Emanuel, M.L. Budarf, D. Driscoll, I. Teshima. The Hospital for Sick Children, Toronto, Ontario, Canada, Abstract 159. *Deletion size was determined in 76 patients with 22q11 deletions using 3 FISH probes. Clinical features were compared to deletion size and no relationship was found between the size of the deletion and the severity of expression of the syndrome.*

Screening cardiac patients for 22q11.2 deletions. D.A. Driscoll, B.S. Emanuel, M.L. Budarf, Children's Hospital of Philadelphia, Philadelphia, PA, Abstract 160. *105 patients with conotruncal anomalies were screened for 22q11 deletions; 13 were deleted. Technique for PCR-based screening was described.*

Evidence implicating the 22q11 region in the development of Wilms tumor associated with VCFS. E.S. Cantú, C.F. Salinas, C. F. Wright, Medical University of South Carolina, Charleston, SC, Abstract 517. *This paper reports a single case of a five year old female with VCFS who had a Wilms tumor (a kidney tumor) detected in infancy. The patient had an unusual variant of the deletion typically found in VCFS. The authors also performed deletion analysis on tissue from the tumor, as well as peripheral blood, and found that an additional marker derived from the mother was deleted from the tumor, but was present in the DNA derived from blood. The authors believe that the deletion of the maternal marker may have unmasked a gene carried by the father which caused the Wilms tumor. The is the first reported case with this rare form of tumor.*

Respiratory infections in children with velo-cardio-facial syndrome. C.K. Cunningham, L.B. Weiner, R.J. Shprintzen, State University of New York Health Science Center at Syracuse, Syracuse, NY, Abstract 528. *In this retrospective analysis of 121 patients with VCFS, the number of hospital admissions and episodes of pneumonia, bronchitis, and middle ear disease were ascertained and plotted over time. Approximately 30% of patients with VCFS were admitted in the first year of life for respiratory infections, approximately 20% the second year, and nearly half that the third year. In the fourth year, half again were admitted to the hospital (approximately 5%) and by age 5, admissions in the VCFS group were rare. Almost all patients admitted after the*

first year of life had been admitted in the first year, whereas only one patient admitted after the first year of life had not been admitted in the first year. This indicates that admissions during the first year represent a significant risk factor for subsequent hospitalizations. The presence of heart disease was also associated with larger numbers of infections, though patients without heart disease were also at risk. Pneumonia, bronchitis, and middle ear disease were all common in the population.

DiGeorge syndrome and CHARGE association in five patients. P. de Lonlay-Debeney, V. Cormier-Daire, J. Amiel, V. Abadie, D. Bonnet, M. Prieur, M. Vehemans, A. Munnich, S. Lyonnet, Hospital Enfants Malade, Paris, France, Abstract 532. *Five patients with DiGeorge sequence and findings consistent with CHARGE association (another etiologically nonspecific multiple anomaly disorder involving heart malformations) are described. None had a 22q11 deletion, nor a 10p13 deletion. Both DiGeorge sequence and CHARGE association are known to occur secondary to VCFS, but in these cases, VCFS was not diagnosed.*

Polysplenia and neutropenia in a patient with 22q11 deletion and trichorhinophalangeal syndrome. Y.S. Fan, A.E.Cairney, V.M. Siu, University of Western Ontario, London, Ontario, Canada, Abstract 542. *A girl is reported who is the child of a mother with trichorhinophalangeal syndrome and a father with velo-cardio-facial syndrome. The child has features of both disorders, but also has neutropenia (a blood disorder) and enlarged spleen with polysplenia. She also had tetralogy of Fallot. The authors suggest that the polysplenia (the second such reported case) may represent a laterality sequence.*

Late presentation of velo-cardio-facial syndrome with hypocalcemic seizures and intracerebral calcification, O. Goker-Alpan, A.L. Gropman, C.J. Tifft, National Human Genome Research Center, Washington, D.C., Abstract 552. *Two cases are reported who had late onset of hypocalcemic seizures during adolescence. Calcifications in the brain were also found which suggested that the hypocalcemia had been occurring for some time.*

22q11.2 microdeletion syndrome associated with aortic root dilatation with or without other cardiac anomalies. D.K. Grange, G.K. Singh, S-C Chen, I.C. Balfour, S.B. Jureidini, S. Nouri, Saint Louis University School of Medicine, St. Louis, MO, Abstract 554. *Thirty patients with VCFS, 27 with known heart anomalies, 3 with no known heart anomalies, were studied for cardiovascular anomalies. Aortic root dilitation was found in 12 of 27 patients who had heart disease, and more importantly, the other three patients without heart anomalies also had aortic root dilation. The authors suggest that all cases with VCFS should be screened for aortic root anomalies.*

Is there a subtype of schizophrenia associated with a chromosome 22q11 deletion and velo-cardio-facial syndrome? K. Hodgkinson, S. Correia, L. Scutt, E. Chow, R. Weksberg, A. Bassett, The Hospital for Sick Children, Toronto, Canada, Abstract 565. *Twenty-five patients were ascertained from a population of patients with schizophrenia based on the presence of a history of learning disabilities, hypernasal speech, heart anomalies, or physical features consistent with VCFS. Twenty of these patients were tested for deletions, and 10 were found to be deleted for 22q11.*

Changes in facial phenotype of chromosome 22q11.2 deletion syndrome with age. H. Kawame, K. Kurosawa, K. Suzuki, A. Katsuka, Y. Ochiai K. Maekawa, Tokyo Metropolitan Kita Medical Rehabilitation Center, Tokyo, Japan, Abstract 575. *The authors present cases illustrating normal facial appearance at birth of patients with VCFS who subsequently develop the characteristic facial appearance so that it becomes recognizable in later childhood (4 or 5 years of age). The point is made that normal appearance at birth makes the early diagnostic process more difficult.*

The Spectrum of the chromosome 22q11 Deletion. D.M. McDonald-McGinn, D. LaRossa, P. Randall, E. Goldmuntz, B.J. Clarke III, K. Sullivan, P. Eicher, D. Lynch, P. Bingham, P. Wang, M. Gerdes, E. Moss, C. Solot, T. Moshang, J.E. Ming, D. Driscoll, B. Emanuel, E.H. Zackai, Children's Hospital of Philadelphia, Phildelphia, PA, Abstract 597. *This poster reports the variety of clinical findings associated with 22q11 deletions, including VCFS, DiGeorge, conotruncal anomalies face syndrome, Opitz syndrome, and isolated conotruncal anomalies.*

Genetic etiologies of velopharyngeal insufficiency. H.M. Saal, T. Ringhand, C.A.Prows, R.J. Hopkin, Children's Hospital Medical Center, Cincinnati, OH, Abstract 626. *84 patients with velopharyngeal insufficiency were evaluated prospectively. Fifty-four (64%) were found to have a genetic disorder, the most common of which was VCFS which was found in 21%.*

Velocardiofacial syndrome (VCFS) and schizophrenia: a cluster analysis of patients and their dymorphic features. L. Scutt, S. Correia, E. Chow, J. Hogan, C. Jones, W.G. Honer, K. Hodgkinson, S. Kaegi, R. Weksberg A.S. Bassett, Queen Street Mental Health Center, Toronto, Ontario, Canada, Abstract 632. *A study was conducted using a specific type of statistical method to link the occurrence of schizophrenia with facial features consistent with velo-cardio-facial syndrome.*

What's in a face? Defining the characteristic facial changes in microdeletion 22q11.2 by cephalometric analysis. J.E. Selnes, R.B. Ross, J. Siegel-Bartelt, The Hospital for Sick Children, Toronto, Ontario, Canada, Abstract 635. *The authors review cephalometric findings in 17 patients. Among the findings were a flat cranial base (platybasia) and a short posterior cranial base.*

Microdeletion 22q11.2: anatomic defects are frequent in the high cervical spine. J. Siegel-Bartelt, D. Armstrong, The Hospital for Sick Children, Toronto, Ontario, Canada, Abstract 637. *X-rays of the cervical spine of 26 patients with VCFS were reviewed. 25 had abnormalities of the high cervical spine, including spina bifida occulta and odontoid subluxation. Only two patients were symptomatic. The authors suggest that cervical spine X-rays should be routine parts of an evaluation.*

Increased incidence of renal anomalies in patients with 22q11 deletion. T.L. Stewart, M.B. Irons, J.M. Cowan, D.W. Bianchi, New England Medical Center, Boston, MA, Abstract 643. *Sixteen cases of VCFS were reviewed, 13 of whom had renal ultrasound studies. Of the 13 patients with renal ultrasounds, 5 had a variety of renal anomalies (38.4%). The authors state that this percentage of renal malformations was higher than expected.*

Dual color interphase FISH analysis for detection of 22q11 deletions. K. May, C. Taylor, B. Bunke, D. Helfrick, Emory University School of Medicine, Atlanta, GA, Abstract 759. *This paper presents a technique for FISH analysis of the 22q11 region using interphase cells rather than a metaphase spread.*

Using mouse models for understanding the genetic basis of human 22q11 microdeletion syndromes. W.L. Kimber, S. Hirotsune, H.F. Sutherland, S. Pack, L. Garrett, A. Chen, P.J. Scambler, A. Winshaw-Boris, National Human Genome Research Institute, Washington, D.C., Abstract 886. *This poster discusses the use of mouse models to study the expression of phenotypes associated with 22q11 deletions in humans.*

Monozygotic twins with chromosome 22q11 deletion and concordant heart defects. L.M. Levitch, D.M. Zimmer, J. Gunter, J. Burlbaw, T. Arthur, L. Hankins, R. Ardinger, D.L. Persons, University of Kansas Medical Center, Kansas City, KS, Abstract 897. *This poster presents identical twins who had the same 22q11.2 deletion and truncus arteriosus.*

Gene encoding neuronal calcium-activated potassium channel has polymorphic CAG repeats, a candidate role in excitotoxic neurodegeneration and maps to 22q11-q13, critical region for bipolar disease and schizophrenia. K.G. Chandy, E. Fantino, K. Kalman, G.A. Gutman, J.J. Gargus, University of California, Irvine, Irvine, CA, Abstract 1783. *The authors present a biochemical pathway for the development of mental illness which lies adjacent to the 22q11 region typically deleted in VCFS. They report the presence of CAG repeats within the human gene. Additional data on the authors' findings was presented in the New Research section during the meeting.*

Chromosome 22q11 deletion: excessive new mutations, biased origin of deletion, and the effect of ethnic background. M-Y Chung, J-H Lu, B-T Hwang, C.C-L Meng, H-P Chien, H. Chiang, Veterans General Hospital, Taipei, Taiwan, R.O.C., Abstract 1788. *Screening of 252 patients with congenital heart disease for 22q11 deletions yielded 19 cases. All except one were new mutations (nonfamilial). The authors conclude that this portion of the genome undergoes frequent rearrangement.*

Incidence and significance of 22q11 hemizygosity in interrupted aortic arch. A. Rauch, M. Hofbeck, G. Leipold, J. Klinger, U. Trautmann, H. Singer, R.A. Pfeiffer, University of Erlangen, Germany, Abstract 1862. *Nine children with type B interrupted aortic arch, and 3 with type A were analyzed with multiple markers within te 22q11 region. None of the type A cases were deleted, but 8 out of nine of the type B cases were deleted. The authors conclude that all patients with type B interrupted aortic arch should be tested for deletions.*

Comparative mapping of the human and mouse VCFS/DGS syntenic region discloses the presence of a large internal rearrangement. A.I. Skoultchi, A. Puech, B. Saint-Jore, B. Funk, N. Copeland, N. Jenkins, R. Pandita, C. Carlson, Hsirotkin, R. Kucherlapati, B.E. Morrow, Albert Einstein College of Medicine, Bronx, NY, Abstract 296. *Comparison of the mouse and human genomes shows that 17 genes from the 22q11.2 critical region are located in one region of the mouse genome on mouse chromosome 16, spanning from DGCR6 to IGL. Synteny is broken at the proximal end from DGCR6 to VHAPTE which is on mouse chromosome 6. At the distal end, synteny is broken with IGL, GNAZ, BCR, and GSTTII mapped to mouse chromosome 10. CLTD was not found in the mouse genome. These findings may help generate better strategies for studying models for VCFS.*

Prenatal diagnosis of VCFS: clinical and counseling issues. J. Ferreira, M. Ben-Yishay, S.J. Gross, V. Puljaal, S. Gogineni, H.M. Nitowsky, B. Morrow, R. Goldberg, R. Marion, Montefiore Medical Center, Bronx, NY, Abstract 871. *A case is reported of prenatal detection of VCFS where the deletion was found in the absence of physical findings on ultrasound.*

A new goosecoid gene family member is in the VCFS/DGS critical region. B. Funke, B. Saint-Jore, A. Puech, H. Sirotkin, S. Raft, C. Carlson, R.K. Pandita, R. Kucherlapati, A. Skoultchi, B.E. Morrow, Abstract 981. *A new homeodomain containing gene, GSCL, was cloned from the critical region in VCFS. The gene is thought to be involved in embryonic development. 17 nondeleted patients with VCFS were assessed for a mutation in the coding region for GSCL, but none were found. However, a polymorphism was found at codon 47 (Arg->Cys).*

Goosecoid-like, a candidate gene for DiGeorge syndrome, is expressed in the developing brain of mouse embryos. S. Gottlieb, N. Galil, J. Epstein, S.D. Hanes, C. Buck, B.S. Emanuel, M.L. Budarf, Children's Hospital of Philadelphia, Philadelphia, Pa, Abstract 990. *A gene is identified which is a member of a subfamily of homeobox proteins in vertebrates.*

Establishment of a transcription map in the 22q11.2 microdeletion syndrome critical region. S. Demczuk, A. Aurias, P. Eydoux, Montreal Children's Hospital, Montreal, Quebec, Canada, Abstract 1355. *A transcription map was constructed based on exon trapping. At least four newly expressed sequences were identified in the critical region.*

Human and murine genomes contain two proline oxidase homologs, one of which maps to DiGeorge/VCFS region and is deficient in the PRO/Re. W-W Lin, C.A. Hu, G. Steet, C. Obie, J. Steet, J. Lund, R. Reeves, J. Rutberg, M. Geraghty, D. Valle, Johns Hopkins University Medical School, Abstract 1492. *Proline oxidase (POX) deficiency is known to cause hyperprolinemia,*

a disorder found in patients with VCFS, often resulting in learning problems and sluggishness. POX2 is reported to map to 22q11.2 and the authors speculate that haploinsufficiency of POX2 may account for some of the VCFS phenotype.

Terminal transverse limb defects in a patient with velo-cardio-facial syndrome (VCFS) and the 22q11.2 deletion. A.R. Mank-Seymour, J.H. Cummins, S. Wenger, C.A. Bay, Children's Hospital of Pittsburgh, Pittsburgh, PA, Abstract 2162. *A single case with hemimelia of the left forearm is described. The authors suggest that limb anomalies may not be reported in many cases of VCFS and that the presence of limb anomalies should lead to consideration for the diagnosis of VCFS.*

Functional analysis of two genes in the velo-cardio-facial syndrome commonly deleted region. A. Puech, H. Sirotkin, B. Saint-Jore, R. Kucherlapati, A.I. Skoultchi, Albert Einstein College of Medicine, Bronx, NY, Abstract 2216. *Mouse knock outs for the genes IDD and Arvcf are described and reported to be viable. Breeding of these mice is being carried out to determine the effect of a null mutation on use development.*

Identification of a novel noncoding nuclear RNA from the DiGeorge syndrome critical region at 22q11. G. Novelli, A. Pizzuti, F. Amati, A. Ratti, A. Mari, I. Fogh, E. Conti, M. Bengala, R. Bordoni, E. Bellone, P. Mandich, A. Colosimo, F. Pandolfi, B. Dallapicolla, Tor Vergata University, Rome, Italy, Abstract 2232. *A new transcript (22K48) is described, identified by cDNA selection on yeast artificial chromosomes mapped to the critical region for VCFS. The transcript is expressed in several cell types. It does not have known homology to currently known sequences. It has high levels of expression in heart and skeletal muscle.*

ANOTHER REMINDER.... THE FOURTH ANNUAL MEETING OF THE VELO-CARDIO-FACIAL SYNDROME WILL BE HELD JUNE 26-28, 1998 IN BOSTON. INFORMATION, PREREGISTRATION FORMS, AND ABSTRACT FORMS WILL BE MAILED TO THE MEMBERSHIP SHORTLY. PLEASE FORWARD ANY PROGRAM SUGGESTIONS TO EITHER THE EXECUTIVE DIRECTOR, ROBERT SHPRINTZEN, OR TO THE PRESIDENT, MAUREEN ANDERSON, AS SOON AS POSSIBLE. DR. SHPRINTZEN'S ADDRESS IS: SUNY HEALTH SCIENCE CENTER AT SYRACUSE, JACOBSEN HALL 707, 750 EAST ADAMS STREET, SYRACUSE, NY 13210, PHONE 315-464-6590, E-mail: shprintr@mailbox.hscsyr.edu. MRS. ANDERSON'S ADDRESS IS 2 LANSING DRIVE, SALEM, NH 03079, PHONE: 603-898-6332, E-mail: mladja@aol.com. *PARTIAL FUNDING IS BEING PROVIDED BY CHILDREN'S HOSPITAL OF BOSTON AND ITS MEDICAL STAFF.*

Minutes, Third Annual Meeting

Membership continues to grow at slightly over 1,000, 80% from the U.S. and Canada, 20% from Europe, Asia, and Australia. The treasury had approximately $3,800 and is expected to remain solvent through 1997. Dues will remain stable. An additional $350 had been received in donations to the Caitlin Lynch Memorial Fund which covered 5 scholarships for the current meeting. Chris and Catherine Lynch and Bob and Nicki Woods were thanked for their generous donations to the Caitlin Lynch Memorial Fund. $310 had been received for the Tony Lipson Memorial Fund to bring someone from the Australian support group to the annual meeting. This could not be done for the 1997 meeting because of insufficient funds, but he was hopeful that someone could be brought to the 1998 meeting. Mary Anne Witzel provided a generous donation to the Lipson Fund. The James A. Meador Foundation was thanked for a donation of $2,000 to help support the annual meeting. This was the second grant from the James A. Meador Foundation which was facilitated by a Foundation member who asked to remain anonymous. The Landsman and the Keleshian families were thanked for generous donations over the past year. The tax exempt status of the Foundation was discussed; Jeff Landsman, a member of the Board of Directors suggested that the Foundation seek its own 501(c)3 status with the IRS. The membership approved by majority vote. The meeting site for 1998 will be Boston. Maureen Anderson who heads the New England support group offered to serve as local arrangements Chair. Milwaukee will be the site for 1999 with future meeting to be held in Baltimore and Toronto. Elections were then held. The following slate was elected:

President: Maureen Anderson (Lay Member, Salem, NH)
Board of Directors: Pam Hunter (Lay Member, Cupertino, CA)
Susan Marks (Professional Member, Milwaukee, WI)
Editor: Deborah Hung Copenheaver (Professional Member, Washington, D.C.)

Liaison Committee Chairperson: Lisa Jennings (Lay Member, Weymouth, MA). The current Executive Council consists of :

Executive Director: Robert J. Shprintzen (Professional Member, Syracuse, NY, term expires 2000)
President: Maureen Anderson (Lay Member, Salem, NH, term expires 1998)
Past President: Harry Keleshian (Greenwich, CT, term expires 1998)
Secretary-Treasurer: Edna Keleshian (Lay Member, Greenwich, CT, term expires 1998)
Editor: Deborah Hung Copenheaver (Professional Member, Washington, D.C., term expires 1999)
Board of Directors: Karen J. Golding-Kushner (Professional Member, East Brunswick, NJ, term expires 1998)
Raju Kucherlapati (Professional Member, Bronx, NY, term expires 1999)
Susan Marks (Professional Member, Milwaukee, WI, term expires 2000)
Jeff Landsman (Lay Member, Madison, WI, term expires 1998)
Lucy Burke (Lay Member, Redwood City, CA, term expires 1999)
Pam Hunter (Lay Member, Cupertino, CA, term expires 2000)

The Foundation will put together a Directory, including email addresses. A vote was taken to determine if the membership would permit their names, addresses, and phone numbers to be distributed to the membership. The entire membership present at the business meeting agreed that this was a good idea.

Information for the VCFSEF Directory:

Please fill in the following information if you would like to be included in the Directory. You may email your information to: ringoldk@mailbox.hscsyr.edu, fax it to 315-464-5321, or mail it to: Kelvin Ringold, C.D.U., Jacobsen Hall, 7th floor, SUNY Health Science Center, 750 E. Adams St., Syracuse, NY 13210.

Name:	Email
Address:	
Preferred telephone:	Fax:
For Lay Members, name, sex, and birth date of relative/friend with VCFS:	
For Professional Members, your area of expertise or study:	
If you belong to a support group, please list it here:	

Upcoming Events... We are developing a VCFS Web Page at the University Hospital site in Syracuse. We plan for it to be a very dynamic site and will have it up and running by the end of the year. Those of you with email ability will be notified via email. One of the benefits we hope to accomplish is having the VCFSEF newsletter available online, and give the membership a choice of having a hard copy mailed or just being notified via the internet when the new issue is online. Simultaneously, we will have a VCFS email address where you can send questions and queries. In the meantime, please make sure we have your current email address. You may send email to: ringoldk@mailbox.hscsyr.edu. Kelvin is Dr. Shprintzen's administrative assistant in Syracuse.

Note: If your household receives multiple copies of this newsletter and you'd prefer to receive just one, please let us know.

Velo-Cardio-Facial Syndrome Educational Foundation
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