Research Publications and selected abstracts of Prof. Dr. Sunny Luke, Academic Director IISAC, USA (www.iisac.org)

Section A: PUBLICATIONS

Luke S. and Mathew B. (2012) Kerala, Farmers' Own Paradise (*text book chapter*) p 779-806. *In* Introduction to Kerala Studies, Volume II. IISAC, New Jersey, USA

Mathew B, **Luke S** and Mani P.K. (2012) Nature's Visual Feast: Ornamental Plants of Tropical Kerala (*text book chapter*) p 807- 834 *In* Introduction to Kerala Studies, Volume II. IISAC, New Jersey, USA

Raman M, **Luke S** and Shaji P.K (2012) Kerala:An Epitome of Tropical Biodiversity (*text book chapter*) p 707-736 *In* Introduction to Kerala Studies, Volume II. IISAC, New Jersey, USA

Luke S. and Cooper L. (2012) Kerala for an Educated Traveler (*text book chapter*) p 49-66. *In* Introduction to Kerala Studies, Volume 1. IISAC, New Jersey, USA

Marx G, Levdansky L, Silberklang M, Thomas D, Hoffman N, **Luke S,** Lesnoy D,gorodetsky R, (2008) :Haptide-coated collagen sponge as a bioactive matrix for tissue regeneration. J Biomed Mater Res 84(2):571-83

Huang NF, Gupta M, **Luke S** (2006): Detection of genetic abnormalities in ovarian carcinomas (*text book chapter*)p 307-332 . *In* Handbook of Immunohistochemistry and *in situ* hybridization of human carcinomas: Molecular Genetics, Gastrointestinal Carcinoma, and Ovarian Carcinoma, Volume 4 Elsevier Sciences Press NY)

Thomas D, Huang NF, **Luke S** (2005): Stem cell therapeutics for cardiac repair.Ind.J.Multi.Res 1 (1): 1-12

Eisenbud D, Haung NF, **Luke S**, Silberklang M (2004): Skin substitutes and wound healing: Current status and challenges. Wounds 16(1): 2 – 17.

Huang NF, Varghese SZ, **Luke S** (2003): Apoptosis in skin wound healing. Wounds 15 (6): 182 – 194.

Huang NF, Gupta M, Varghease S, Rao S, **Luke S** (2002): Detection of numerical chromosomal abnormalities in epithelial ovarian neoplasms by fluorescence *in situ* hybridization and a review of the literature. Appl. Immunhistochem & Mol Morph 10(2): 187- 193.

Xia J, Gupta M, Preminger B, Varkey JA, **Luke S** (1999): Small cell carcinoma of the ureter arising in an adult polycystic kidney. A case report with interphase cytogenetics study. Appl. Immunhistochem & Mol. Morph 7: 164 – 168.

Luke S, Varkey JA, Belogolovkin V, Ladoulis CT(1997): The current state of the fluorescence *in situ* hybridization (FISH) in diagnostic pathology. Cell Vision 4: 2-17

Luke S, Belogolovkin V, Varkey JA, Ladoulis CT (1997): Fluorescence in situ hybridization (*text book chapter*) p139 –173. In Analytical Morphology, Eaton Publications, MA.

Luke S, Gandhi S, Verma RS (1995): Conservation of DNA synteny of Down syndrome critical region in human and great apes. Gene 161(2): 283-285

Luke S, Verma RS (1995): The genomic sequence for Prader-Willi/ Angelman syndromes loci of human are apparently conserved in the great apes. J Mol. Evol. 41: 250- 252

Luke S, Verma RS (1995): Human and Chimpanzee share ancestral centromeric alpha satellite DNA sequences but other fractions of heterochromatin differ considerably. Am J Phy. Antro. 96: 63 – 71

Conte RA, **Luke S,** Verma RS (1995): Enumeration of seminal leukocytes by fluorescence in situ hybridization.

Conte RA, **Luke S,** Verma RS (1995): Characterization of ring chromosome 21 by FISH technique. Clin Genet 48 (4): 188 – 191

Verma RS, **Luke S,** Conte RA (1994): Fish technique: what's all the fuss about. Genet. Anal. Tech. Appl 11 (4): 106 – 109.

Verma RS, **Luke S** (1994): Evolutionary divergence of human chromosome 9 as revealed by the position of ABL protooncogene in higher primates. Mol.General Genet 243 (4): 369-373.

Luke S, Birnbaum R, Verma RS (1994): A double hybridization for localization of centromeric and telomeric repeat sequences in nonagenarians. Genet. Anal.Tech. Appl 11(3): 77 – 80

Luke S, Verma RS, Conte RA, Luke S (1994): Identification of Prader – Willi Locus in an isodicentric marker chromosomes. Am.J.Med. Genet 51: 232 – 233

Verma RS, Giridharin R, Conte RA, **Luke S** (1994): An apparent balanced translocation between chromosomes 7 and 13 in a 47, XYY individual. Jpn J Hum Genet 39 (4): 451-452

Verma RS, Conte RA, Mathews T**, Luke S** (1994): Monozygotic twinning in a female with triple X (47, XXX). Gynecol Invest 37: 279 – 280.

Luke S, Aggarwal G, Stetka DG, Verma RS (1994): Alphoid diversity of a so called monocentric Robertsoninan fusion. Chromo Res 2: 73-75

Luke S, Verma RS (1993): The genomic synteny at DNA level between human and chimpanzee chromosomes. Chromo. Res 1: 215 – 219.

Verma RS**, Luke S**, Brennan JP, Matthews T, Conte RA, Macera MJ (1993): Molecular topography of the secondary constriction region (qh) of human chromosome 9 with unusual euchromatic band . Am.J.Hum. Genet 52: 981- 986

Luke S, Verma RS (1993): Telomeric repeat (TTAGG) sequences of human chromosomes are conserved in chimpanzee. Mol. Gen 237: 460 – 462.

Luke S, Verma RS (1993): Telomeric repeat (TTAGGG)n sequences of human chromosomes are conserved in chimpanzee. Mol.Gen.Genet 237: 460 – 462.

Luke S, Verma RS (1993): Genet consequences of euchromatic band within 9qh region. Am J.Med. Genet 45: 107

Luke S, Verma RS (1992): Chromosomal domains of chimpanzee are diverged from human as revealed by in situ hybridization using human genomic probe. Hum. .Evol. 7: 71-74.

Verma RS, **Luke S,** Conte RA (1992): Molecular characterization of the smallest secondary constriction region (qh) of the human chromosome 16.GATA 9: 140-142

Luke S, Verma RS, Conte RA, Mathews T (1992): Molecular characterization of the secondary constriction region of the human inverted chromosome 9 by fluorescence in situ hybridization. J. Cell Sci 103 (4): 919-923

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Luke S, Mathews T, Verma RS (1992): Evolution of pericentromeric heterochromatin of human X-chromosome. Genetica 87: 63-64

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Conte RA, **Luke S,** Verma RS (1992): Molecular characterization of inverted pericentromeric heterochromatin of chromosome 3. Histochemistry 97: 509-510

Luke S, Verma RS (1992): Detection of the heteromorphic spectrum of heterochromatin in the human genome by in situ digestion using restriction endonuclease Alu1. Am. J. Med Genet 43: 1026 – 1029.

Verma RS, Conte RA, Pitter JH**, Luke S** (1992): A rare chromosomal abnormality involving pericentric inversion of chromosome 7 and ring chromosome 8 in a girl with minor anomalies J. Med. Genet 29: 66-67.

Luke S, Bennett HS, Pitter JH, Verma RS (1992): A new case of monosomy for 17q25 qter due to a maternal translocation[t(3;17) p12;q24] Ann. Genet 35: 48-50.

Verma RS, **Luke S**, Dhawan P (1992): Twins with two different fathers. Lancet 339: 63-64.

Verma RS, **Luke S** (1991): Heteromorphisms of pericentromeric heterochromatin of chromosome 19. GATA 8 (6): 179-180

Luke S, Verma RS (1991): Pericentromeric heterochromation of chromosome 3. J.Med.Genet 28: 805 –808

Verma RS, **Luke S,** Conte RA, Macera MJ (1991): A so called rare heteromorphism of the human genome. CytogenetCell Genet 56: 63

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Luke S, Verma RS, PeBenito R, Macera MJ (1991): Inversion-duplication of bands q13-q21 of human chromosome 9. Am J Med Genet 40: 57 –60.

Section B: INTERNATIONAL PRESENTATIONS

Luke S, Tewari R, Silberklang M (2004): Development and validation of a histological assay for tissue engineered *OrCel* Bilayered Cellular Matrix (*Presentation @ Biomedical Engineering Society Annual Meeting in Philadelphia)*

Chimanji N, Tewari R, **Luke S**, Silberklang M (2004): *In vitro* evidence for the histocompatibility of the allogenic cells in cultured skin substitutes, *OrCel* Bilayered Cellular Matrix (*Presentation @ Biomedical Engineering Society Annual Meeting in Philadelphia)*

Windsor M, Wilson C, Tewari R, Cimanji N, **Luke S,** Eisenberg M, Moore G, Philip M, Silberklang M (2004): A novel healing model in the SCID mouse applied to the therapeutic cultured device, *OrCel* – Bilayered Cellular Matrix (*Presentation @ Biomedical Engineering Society Annual Meeting in Philadelphia)*

Huang N F, Chimanji N, **Luke S,** Silberklang M, Eisenbud D (2004: Emerging biological therapeutics in chronic ulcer management (*Presentation @ Biomedical Engineering Society Annual Meeting in Philadelphia)*

Tewari R, **Luke S,** Lesnoy D, Burke T, Silberklang M (2004): Histological Analysis of the Collagen sponge component of a tissue engineered skin substitute (*Presentation @ Biomedical Engineering Society Annual Meeting in Philadelphia)*

Chimanji N, Tewari R, **Luke S,** Silberklang M (2004): In vitro evidence for the histocompatibility of the allogenic cells in a cultured skin substitute, *OrCel* Bilayered Cellular Matrix (*Presentation @ 19th Symposium for Advanced Wound Care in Orlando FL)*

Windsor M, Wilson C, Tewari R, Chimanji N, **Luke S,** Eisenberg M, Moore G, Philip M, Silberklang M (2003). A novel healing model in the SCID mouse applied to the therapeutic cultured cell device, *OrCel* – Bilayered Cellular Matrix (*Presentation @ 5th International Tissue Engineering Society Meeting in Orlando, Florida)*

Luke S, Xia J, Thomas R, Chaudhri P, Gupta M, Ladoulis CT (1998): Comparison of flow cytometry *Vs* AgNOR for estimating DNA aneuploidy and cell proliferation in breast carcinoma. (*Presentation @ 3rd Annual Multidisciplinary Symposium on Breast Disease, Amelia Island, Florida*)

Varkey JA**, Luke S**, Xia J, Gupta M, Ladoulis CT (1998): Analysis of the rate of proliferation and apoptotic index in human lobular breast carcinomas (*Presentation @ 3rd Annual Multidisciplinary Symposium on Breast Diseases, Amelia Island, Florida*)

Luke S, Thomas R, Chaudhari P, Xia J, Gupta M, Ladoulis C (1997): Correlation of

c-erb B2 gene amplification and chromosomal aneuploidy in ductal carcinoma of the breast. Am. J. Clin Path 107: 479 (*Presentation @ American Society of Clinical Pathologists, Chicago)*

Luke S, Thomas R, Chaudhari P, Xia J, Gupta M, Ladoulis C (1997): Chromosomal Aneuploidy detected by fluorescence in situ hybridization (FISH) in in situ ductal carcinoma of the breast. Am. J. Clin. Path 107: 479 *(Presentation @ American Society of Clinical Pathologists)*

Varkey JA, Chaudhari P, Gupta M**,** **Luke S**, Ladoulis CT (1997): Molecular histopathological analysis of signet cell carcinoma of the sigmoid colon.Am J. Hum. Genet 47: 2113

Luke S, Shepelsky M (1997): FISH: recent advances and diagnostic aspects.(Presentation @ International Conference on Molecular Morphology at University of Florida, Proc 36-40)

Luke S, Huang NF, Goyal N, Varkey JA, Oculam AA, Gupta M, Ladoulis CT (1997): Optimization of fluorescence in situ hybridization in cytological specimens (*Presentation @ International Conference on Molecular Morphology at University of Florida,* Proc 84-85)

Menon S, **Luke S**, Solish G (1995): Polymorphism and cross hybridization – pitfalls in aneuploidy enumeration by fluorescence in situ hybridization. Am J. Clin Path 104 (3) 328 (*Presentation @ American Society of Clinical Pathologists*)

Lester P, **Luke S,** Verma RS (1993): A novel method for estimating interphase stages using human genomic painting. Am. J. Hum. Genet 53(3): A576

Agarwal G, **Luke S,** Verma RS (1993): Hybridization spectrum of the human genome using chromosomes 13/21 alphoid probe. Am. J. Hum. Genet 53 (3): A521.

Conte RA, **Luke S**, Verma RS (1993): Molecular characterization of a ring chromosome 21 in a Down syndrome. Am. J. Hum. Genet 53 (3): A536.

Girisdharan R, Conte RA, **Luke S**, Macera MJ, Verma RS (1993): Molecular characterization of a marker chromosome in an individual with hypotonia and global developmental delay. Am. J. Hum. Genet 53 (3): A551

Luke S, Verma RS (1993): Evolutional mechanism of Prader-Willi locus through inversion in chimpanzee. Am. J. Hum. Genet 53 (3): A 874

Brennan JP, Verma RS, **Luke S,** Conte RA, Macera MJ (1992): Origin of extra G-positive band within the 9qh region. Am. J. Hum. Genet 51(4): A 1232

Mathew T, **Luke S**, Verma RS (1992): Rapid diagnosis of chromosomal abnormalities in fetal loss. Am. J. Hum. Genet 51 (4) A1622

Verma RS, **Luke S** (1992): Pitfalls of fluorescence in situ hybridization. Am. J. Hum. Genet 51 (4) A 154

Section C: SAMPLE ABSTRACTS OF DR.SUNNY LUKE

1. Luke S, Verma RS (1995): Human and Chimpanzee share ancestral centromeric alpha satellite DNA sequences but other fractions of heterochromatin differ considerably. Am J Phy. Antro. 96: 63 – 71

The *euchromatic* regions of chimpanzee (*Pan troglodytes*) genome share approximately 98% sequence similarity with the human (*Homo sapiens*), while the *heterochromatic* regions display considerable divergence. Positive heterochromatic regions revealed by the CBG-technique are confined to pericentromeric areas in humans, while in chimpanzees, these regions are pericentromeric, telomeric, and intercalary. When human chromosomes are digested with restriction endonuclease *Alu*I and stained by Giemsa (*Alu*I/Giemsa), positive heterochromatin is detected only in the pericentromeric regions, while in chimpanzee, telomeric, pericentromeric, and in some chromosomes both telomeric and centromeric, regions are positive. The DA/DAPI technique further revealed extensive cytochemical heterogeneity of heterochromatin in both species. Nevertheless, the fluorescence in situ hybridization technique (FISH) using a centromeric alpha satellite cocktail probe revealed that both primates share similar pericentromeric alpha satellite DNA sequences. Furthermore, cross-hybridization experiments using chromosomes of gorilla (*Gorilla gorilla*) and orangutan (*Pongo pygmaeus*) suggest that the alphoid repeats of human and great apes are highly conserved, implying that these repeat families were present in their common ancestor. Nevertheless, the orangutan's chromosome 9 did not cross-hybridize with human probe.

2. Luke S, Gandhi S, Verma RS (1995): Conservation of DNA synteny of Down syndrome critical region in human and great apes. Gene 161(2): 283-285

A quarter century ago, a chimpanzee with trisomy 22 was reported to have the clinical manifestation of Down syndrome. The features of Down syndrome in human have been associated with chromosome 21 band q22.3. The recent availability of chromosome and loci specific probes has prompted us to utilize the human cosmid probe (D21S65) for the trisomy 21 region in the chromosomes of the chimpanzee (Pan troglodytes), gorilla (Gorilla gorilla) and orangutan (Pongo pygmeus). Interestingly, the hybridization site for the Down syndrome region was found on the equivalent ape chromosome 22 in all three primates (the human equivalent of chromosome 21). Apparently, these results support the notion that the Down syndrome critical region of human chromosome 21 band q22.3 is conserved in great apes, which has displayed mongolism in a chimpanzee when present in triplicate conditions. Furthermore, other probes can be used as phylogenetic signals to enhance the understanding of human descent.

3. Luke S, Verma RS (1995): The genomic sequence for Prader-Willi/ Angelman syndromes loci of human are apparently conserved in the great apes. J Mol. Evol. 41: 250- 252

Chromosomal changes through pericentric inversions play an important role in the origin of species. Certain pericentric inversions are too minute to be detected cytogenetically, thus hindering the complete reconstruction of hominoid phylogeny. The advent of the fluorescence in situ hybridization (FISH) technique has facilitated the identification of many chromosomal segments, even at the single gene level. Therefore the cosmid probe for Prader-Willi (PWS)/Angelman syndrome to the loci on human chromosome 15 [q11-13] is being used as a marker to highlight the complementary sequence in higher primates. We hybridized metaphase chromosomes of chimpanzee (PTR), gorilla (GGO), and orangutan (PPY) with this probe (Oncor) to characterize the chromosomal segments because the nature of these pericentric inversions remains relatively unknown. Our observations suggest that a pericentric inversion has occurred in chimpanzee chromosome (PTR 16) which corresponds to human chromosome 15 at PTR 16 band p11-12, while in gorilla (GGO 15) and orangutan (PPY 16) the bands q11-13 complemented to human chromosome 15 band q11-13. This approach has proven to be a better avenue to characterize the pericentric inversions which have apparently occurred during human evolution. "Genetic" divergence in the speciation process which occurs through "chromosomal" rearrangement needs to be reevaluated and further explored using newer techniques.

4. Verma RS, Luke S (1994): Evolutionary divergence of human chromosome 9 as revealed by the position of ABL protooncogene in higher primates. Mol.General Genet 243 (4): 369-373.

Attempts to solve the fundamental questions regarding the descent of man are dogged by superstitions and unexamined orthodoxies. The origin of humans, established a decade ago based upon cytological analysis of ape chromosomes, continues to be called into question. Although molecular methods have provided a framework for tracing the paths of human evolution, conclusive evidence remains elusive. We have used a single ABL gene probe derived from human chromosome 9 to assess the direction of change in the equivalent ape chromosomes. This approach has resulted in a few surprises which again challenge the prevailing view of early primate evolution based solely on chromosome banding patterns. The ABL proto-oncogene is present on human chromosome 9 at band q34. Similar DNA sequences presumed to represent an ABL gene, are present on chromosome 11 in chimpanzee (Pan troglodytes) but at a different relative location, indicating that the mechanism of the origin of

human chromosome 9 is far more complex than has previously been suggested. Nevertheless, in gorilla (Gorilla gorilla) and orangutan (Pongo pygmaeus), the equivalent to human chromosome band 9 q34 is apparently located on chromosome 13 at a putative telomeric position and no discernible differences could be established. Despite the presence of the ABL protooncogene on human equivalent ape chromosomes, molecular systematics will continue to generate enigmas in the evolutionary context until the entire genome is sequenced.

5. Luke S, Verma RS (1993): The genomic synteny at DNA level between human and chimpanzee chromosomes. Chromo. Res 1: 215 – 219.

The evolutionary relationship between human (Homo sapiens) and chimpanzee (Pan troglodytes) has been the subject of debate and scrutiny for over two decades. The close relationship established by numerous parameters may or may not reflect homology at the DNA level. The recent advent of a molecular method termed the chromosome in situ suppression hybridization (CISS)-technique has prompted us to explore the phylogenetic relationship at the DNA sequence level. Cross-hybridization data using human-derived whole chromosome paints (WCPs) suggests an apparent genomic synteny with chimpanzee chromosomes at the DNA level, thus providing a better understanding of an evolutionary relationship between humans and chimpanzees.

6. Luke S, Verma RS (1993): Telomeric repeat (TTAGG) sequences of human chromosomes are conserved in chimpanzee. Mol. Gen 237: 460 – 462.

Using a series of genetic parameters, attempts have been made for more than two decades to establish the close kinship of human (Homo sapiens) with chimpanzee (Pan troglodytes). Molecular and cytogenetic data presently suggest that the two species are closely related. The recent isolation of a human telomeric probe (P5097-B.5) has prompted us to cross hybridize it to chimpanzee chromosomes in order to explore convergence and/or divergence of the telomeric repeat sequences (TTAGGG)n. On hybridization, the human probe bound to both ends (telomeres) of chimpanzee chromosomes, suggesting a concerted evolution of tandemly repeated short simple sequences (TTAGGG)n. Even the terminal heterochromatin of chimpanzee chromosomes was found to be endowed with telomeric repeats, suggesting that evolution of heterochromatin and capping with tandemly repeated short sequences are highly complex phenomena.

7. Conte RA, Luke S, Verma RS (1995): Enumeration of seminal leukocytes by fluorescence in situ hybridization. Clin Genet. 1995 Oct;48(4):188-91.

Aim—To determine whether the fluorescent in situ hybridisation technique (FISH) using a total human DNA genomic probe can be used to enumerate semen leucocytes.

Methods—Semen samples from five donors were subjected to a mild KC1 solution. These samples were then biotin labelled under FISH conditions using a total human DNA genomic

probe and the leucocyte counts were determined. To check the accuracy of the technique a monoclonal antibody against the common leucocyte antigen CD45 [KC56(T-200)] served as a control. An isotypic control for [KC56(T-200)], the immunoglobulin [MsIgG1], served as a secondary control.

Results—Semen leucocytes stained by the FISH technique were easily detected because of their distinct bright yellow colour, while the sperm cells were red. The leucocyte count ranged from 0·5 to 4·9 × 10^6 per ml of semen. KC56(T-200) and its isotypic control MsIgG1, which served as control for the FISH technique, accurately identified 94% and 97% of the semen leucocytes of a control donor, respectively.

Conclusions—The FISH technique using a total human DNA probe can accurately and effectively enumerate the overall leucocyte population in semen.

8. Verma RS, Luke S, Brennan JP, Matthews T, Conte RA, Macera MJ (1993): Molecular topography of the secondary constriction region (qh) of human chromosome 9 with unusual euchromatic band . Am.J.Hum. Genet 52: 981- 986

Heterochromatin confined to pericentromeric (c) and secondary constriction (qh) regions plays a major role in morphological variation of chromosome 9, because of its size and affinity for pericentric inversion. Consequently, pairing at pachytene may lead to some disturbances between homologous chromosomes having such extreme variations and may result in abnormalities involving bands adjacent to the qh region. We encountered such a case, where a G-positive band has originated de novo, suggesting a maternal origin from the chromosome 9 that has had a complete pericentric inversion. In previously reported cases, the presence of an extra G-positive band within the 9qh region has been familial, and in the majority of those cases it was not associated with any clinical consequences. Therefore, this anomaly has been referred to as a "rare" variant. The qh region consists of a mixture of various tandemly repeated DNA sequences, and routine banding techniques have failed to characterize the origin of this extra genetic material. By the chromosome in situ suppression hybridization technique using whole chromosome paint, the probe annealed with the extra G-band, suggesting a euchromatic origin from chromosome 9, presumably band p12. By the fluorescence in situ hybridization technique using alpha- and beta-satellite probes, the dicentric nature was further revealed, supporting the concept of unequal crossing-over during maternal meiosis I, which could account for a duplication of the h region. The G-positive band most likely became genetically inert when it was sandwiched between two blocks of heterochromatin, resulting in a phenotypically normal child. Therefore, an earlier hypothesis, suggesting its origin from heterochromatin through so-called euchromatinization, is refuted here.

9. Luke S, Verma RS (1992): Detection of the heteromorphic spectrum of heterochromatin in the human genome by in situ digestion using restriction endonuclease Alu1. Am. J. Med Genet 43: 1026 – 1029.

A battery of selective banding techniques has been utilized to identify the heteromorphic markers in the human genome. The recent addition of the AluI/Giemsa (G)-technique has helped not only in identifying the variable sites, but in characterizing their heteromorphic spectra. In the present investigation, we classified the pericentromeric heterochromatin by the AluI/G-technique by its size and position using 50 normal individuals and suggested the potential uses of this banding technique over earlier methods

10. Luke S, Verma RS, PeBenito R, Macera MJ (1991): Inversion-duplication of bands q13-q21 of human chromosome 9. Am J Med Genet 40: 57 –60.

Structural abnormalities involving heterochromatic regions of the human genome are difficult to characterize because these segments are G-band negative by GTG technique, a routinely used procedure in clinical cytogenetic laboratories. Chromosome abnormalities of such cases have gone undetected or were incorrectly characterized because these regions are so-called heteromorphisms or variants. Consequently, much anxiety has been aroused by the confusion between a chromosome abnormality and a normal heteromorphic variant. We report the first documented case with a so-called highly unusual h region of chromosome 9 which is not a variation but a structural rearrangement involving a paracentric inversion and a duplication. The major clinical features were psychomotor retardation, microcephaly, narrow palpebral fissures, renal and genital anomalies, vertebral anomalies, protruding tongue, and learning and behavioral problems. A concise review of variable duplicated segments of 9q is also provided.

11. Luke S, Verma RS, Conte RA, Mathews T (1992): Molecular characterization of the secondary constriction region of the human inverted chromosome 9 by fluorescence in situ hybridization. J. Cell Sci 103 (4): 919-923

Pericentric inversion of the secondary constriction region (qh) of human chromosome 9 is a frequent occurrence. This structural alteration is regarded as a normal familial variant, termed heteromorphism, and is inherited in a Mendelian fashion without any apparent phenotypic consequences. We characterized the qh region of chromosome 9 from five individuals using a series of molecular cytogenetic techniques. Four out of the five individuals have an additional area composed of alphoid DNA sequences on the inverted chromosome 9 while one case was found to have an apparently intact alphoid DNA sequence. Although the direct function(s) of alphoid DNA sequences remain unclear, the centromeric breakage involving these sequences in inverted chromosome 9 raises a series of questions pertaining to the monocentric, dicentric

and pseudodicentric nature of pericentric inversions. Nevertheless, these findings have prompted us to suggest that the structural organization of alphoid DNA sequences of the centromeric region of chromosome 9 are apparently "breakage prone" and may be associated with a higher incidence of pericentric inversions. Furthermore, the hierarchical organization of various satellite DNA families (alpha-satellite, beta-satellite and satellite III) within the primary and secondary constriction regions of chromosomes 9 are elucidated here.

12. Eisenbud D, Haung NF, Luke S, Silberklang M (2004): Skin substitutes and wound healing: Current status and challenges. Wounds 16(1): 2 – 17.

Bioengineered skin substitutes have emerged over the past 20 years as the most carefully studied and proven of the advanced wound management technologies. While the initial impetus for their development was to replace autograft, allograft, and xenograft in burn applications, they have found even wider application in the treatment of chronic venous and chronic diabetic ulcers. The current review addresses the history of skin substitutes, surveys the landscape of existing Food and Drug Administration-approved products and other promising innovations that appear close to market, and discusses the reasoning and controversies associated with design of these products. While acellular biologic constructs are discussed, the authors focus on products that include autologous or allogeneic cells. The various clinical trials supporting the use of skin substitutes for different wound healing indications are reviewed. The preponderance of literature supports the cost effectiveness of using skin substitutes in healing burn, autograft donor site, diabetic, and venous wounds. In addition, better methods for early identification of diabetic and venous ulcers that may not heal well with standard treatment should improve the process of triaging candidates for skin substitute therapy. In the future, attaining a more detailed understanding of the mechanisms by which skin substitutes induce accelerated healing, including a better appreciation of the roles of cytokines and cell scaffolds, may lead to product enhancements that increase efficacy. Ongoing progress toward overcoming issues, such as abbreviated shelf life and distribution difficulties, as well as high manufacturing costs, should enable broader implementation of skin substitutes in acute and chronic wound therapy

13. Huang NF, Varghese SZ, Luke S (2003): Apoptosis in skin wound healing. Wounds 15 (6): 182 – 194.

Apoptosis is a highly conserved physiological cell death process that removes unwanted cells. [1,2] Since 1972 when Kerr, et al., introduced the term apoptosis to distinguish from necrosis, there has been tremendous interest in programmed cell death as a critical component in maintaining homeostasis and growth in tissues.[3] Failure of apoptosis can lead to a variety of cancers, viral infections, and autoimmune diseases.[4–6] Since the past three decades when the

mystery of this cellular phenomenon began to unravel, scientists have discovered its valuable applications in clinical research and biotechnology. One area of particular importance is the wound healing process in which apoptosis is responsible for the removal of inflammatory cells and granulation tissue.[7] While extensive literature in apoptosis has been published in many fields, very few have focused on the role of apoptosis in the skin wound healing process.[8,9] This review describes the basic cellular and biochemical aspects of apoptosis and the occurrence of apoptosis during the skin wound healing and regeneration process.

14. Huang NF, Gupta M, Varghease S, Rao S, Luke S (2002): Detection of numerical chromosomal abnormalities in epithelial ovarian neoplasms by fluorescence *in situ* hybridization and a review of the literature. Appl. Immunhistochem & Mol Morph 10(2): 187- 193.

Preliminary retrospective chromosomal analysis was performed using fluorescence in situ hybridization (FISH) with alphoid DNA probes for chromosomes 1, 3, 6, 8, 12, 17, and X. Twenty-four epithelial ovarian tumors were examined in this pilot study, including 8 borderline (LMP) serous tumors, 9 serous carcinoma, and 7 mucinous carcinoma. Hybridization signals were counted to demonstrate the frequency of aneusomy, trace chromosomal progression, and identify the predominance of chromosome copy number abnormalities that are specific to a particular histotype.

The preliminary results revealed almost an equal number of mean aneusomies in serous (58.13 +/- 13%) and mucinous (64.33 +/- 10%) carcinoma, both of which were slightly higher than borderline serous tumors (50.57 +/- 17%). Hyposomies 3 and X were significantly higher in mucinous than in serous ovarian carcinomas, and lowest in borderline serous tumors ($P<0.05$ and $P<0.01$). Signal losses were a more frequent abnormality in all three histologic subtypes. Mucinous carcinomas showed a loss of chromosomes 8 (45.00 +/- 28%) and 3 (43.14 +/- 16%), in addition to a loss of chromosome X (56.29 +/- 12%). Serous carcinomas showed a gain of chromosome 1 (39.44 +/- 32%), followed by losses of chromosomes 6 (37.00 +/- 20%), 17 (36.44 +/- 19%), and 8 (36.89 +/- 19%). In borderline serous tumors, the most frequent findings were losses of chromosomes 6 (38.00 +/- 17%), 12 (36.88 +/- 17%), and 3 (36.13 +/- 21%). However, further research is necessary to substantiate these preliminary results and elucidate their clinical significance. A brief review of the literature pertaining to interphase cytogenetics in ovarian epithelial tumors is discussed also.

15. Marx G, Levdansky L, Silberklang M, Thomas D, Hoffman N, Luke S, Lesnoy D,gorodetsky R, (2008) :Haptide-coated collagen sponge as a bioactive matrix for tissue regeneration. J Biomed Mater Res 84(2):571-83

We previously described a new class of conserved, cell adhesive (haptotactic) peptides, termed Haptides, based on sequences first identified in fibrinogen. Here, we describe a new biomaterial, Haptide-coated Collagen, in which the carbodiimide reagent, EDC, was used to covalently couple a Haptide (preC gamma), equivalent to the carboxy terminus of the fibrinogen gamma chain, to a cross-linked sponge composed of bovine collagen type I. The dose response of Haptide bound to collagen on cell attachment response reached a plateau at a concentration of 5-10 mg Haptide/g collagen.

The Haptized-collagen was more stable to 1N NaOH, with a degradation half-time (T(1/2)) of 1.7 h, compared to 0.9 h for untreated control. Haptized collagen discs could be loaded with approximately 30% more human dermal fibroblasts or bovine aortic endothelial cells than unmodified collagen discs ($p < 0.001$). After a proliferation phase, Haptized collagen discs contained approximately 45% more fibroblasts than non-Haptized discs ($p < 0.01$). Histological analysis following sub-dermal implantation in rats indicated that at day 8, Haptized collagen sponge was less degraded than unmodified collagen sponge, attracted more endogenous fibroblasts with newly deposited collagen, and provoked less inflammatory or other adverse reactions. These results suggest potential clinical applications for Haptized collagen sponge for tissue regeneration, soft tissue augmentation, skin repair, and wound healing.