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Sequence characterization of the $-^{THAI}$ allele of α-thalassemia and rapid detection using a single-tube multiplex-PCR assay. Samuel S. Chong[1,2], Corinne D. Boehm[2], Garry R. Cutting[2], and Douglas R. Higgs[3]. [1]National Univ. of Singapore, Singapore, [2]Johns Hopkins School of Medicine, Baltimore, MD, and [3]Institute of Molecular Medicine, Oxford, England.

Alpha thalassemia is the most common inherited hemoglobinopathy in the world. It is caused most frequently by deletion of one or both *cis*-linked copies of the α-globin gene on chromosome 16p13.3. The most common deletions observed in Southeast Asia are the $-^{SEA}$ and $-^{FIL}$ double-gene deletions, and the $-\alpha^{3.7}$ and $-\alpha^{4.2}$ single-gene deletions. Double-gene deletions *in cis* are clinically significant because homozygosity or compound heterozygosity for such deletions is incompatible with post-natal life. In addition to the well-characterized $-^{SEA}$ and $-^{FIL}$ double-gene deletions, a third double-gene deletion, $-^{THAI}$, has been described. Although a high incidence of the $-^{THAI}$ allele has been reported in Taiwan, it was recently pointed out that the Taiwanese patients in fact have the $-^{FIL}$ allele. We have now sequenced the breakpoint junction of the $-^{THAI}$ determinant of α-thalassemia. The results are consistent with previous mapping data and confirm that the $-^{THAI}$ allele is distinct from the $-^{FIL}$ allele, with the breakpoints of the former encompassing those of the latter. We have incorporated rapid PCR-based testing for this allele into a single-tube multiplex-PCR assay capable of also simultaneously detecting $-^{FIL}$, $-^{SEA}$, and the $-\alpha^{4.2}$ and $-\alpha^{3.7}$ single-gene deletions.

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BRCA buccal immunoassay predicts BRCA1 and BRCA2 mutations. Cohn GM[1], Byrne TJ[2], Hoffman DE[1], Adams LA[1], Lane MA[1], Reece MT[1].
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Approximately 4% of unaffected, reproductive age women have a significant family history for heritable breast or ovarian cancer. While, BRCA1 and BRCA2 (BRCA) mutation analysis may prove useful in the clinical management of such individuals, such testing is prohibitively expensive. We have developed a rapid, noninvasive, and inexpensive, assay capable of identifying BRCA mutations in buccal cells.
Objective: To determine the predictive value of the BRCA buccal immunoassay in the detection BRCA gene mutations.
Methods: Buccal cells and peripheral blood were collected from 11 individuals, identified with a greater than 40% risk of carrying a BRCA mutation. To detect protein truncations which are associated with 90% of BRCA mutations, buccal cells were evaluated for BRCA immunoreactivity. Specifically, a qualitative, immunohistochemical comparison using antibodies directed against the amino and carboxy ends of either BRCA proteins, was performed. The presence of diminished immunoreactivity (total or diminished anti-carboxy reactivity relative to anti-amino reactivity) was scored as predictive for mutation. This analysis was compared to the results of BRCA DNA analysis.
Results: Of the 11 individuals identified, six were found to have a BRCA1 mutation, two were found to have a BRCA2 mutation, and three were found to carry no mutations at all. The BRCA buccal immunoassay correctly predicted the presence of all eight mutations. Of the three individuals without BRCA mutations, immunoassay correctly predicted no mutation for BRCA1 in all three, while correctly predicting the absence of a BRCA2 mutation in 2 of three individuals.
Conclusions: The positive and negative predictive values for this assay were 89% and 100% respectively, suggesting great promise as an inexpensive screen for BRCA mutations.

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Variant chromosome 1 reveals centromeric DNA sequences within the 1qh region. R.A. Conte[1] and R.S. Verma.[2] [1]The Long Island College Hospital, Brooklyn, NY, [2]Wycoff Heights Medical Center, Brooklyn - New York Hospital-Weill Medical College of Cornell University, NY and SUNY Health Science Center at Brooklyn, NY.

Adjacent fractions of human genomic heterochromatin may contain distinct DNA sequence families that can be characterized by a number of molecular and conventional procedures. GTG banded metaphase chromosomes from amniocytes revealed a chromosome 1 with a large heterochromatic region that was lightly stained by Giemsa, it's homologue had a small 1qh region that stained dark. The 1qh region of both homologues stained dark by the *AluI*/Giemsa technique. The *TaqI*/Giemsa procedure, which completely digested the 1qh of the normal homologue, did not fully digest the variant's 1qh. A whole chromosome 1 painting probe did not produce any signals in the 1qh of both homologues. The chromosome 1 alphoid centromeric probe showed signals that covered the entire 1qh of the variant homologue and displayed signals that were localized to the centromeric region in the normal variant. It has been shown that chromosome 9 beta satellite DNA sequences have related sequences that are harbored within the pericentromeric region of chromosome 1. A chromosome 9 specific beta satellite probe demonstrated positive signals within the entire 1qh of the variant and presented signals localized to the centromeric region in the normal homologue. These data suggests that the variant 1qh region apparently contains amplified chromosome 1 alpha and sequences related to chromosome 9 beta satellite DNA.

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X-Linked Corneal Dermoids Maps to Xq24-Xter

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Corneal Dermoid (CD, MIM#304730) is a rare congenital tumor confined to the cornea. The tumor is composed of ecto-dermal and mesodermal tissues combined in different proportions. Most cases are sporadic and unilateral. We have studied a unique family, originally described by our center, of which only males presented with bilateral central corneal opacification at birth with no other systemic abnormalities. Histological feature consisted mainly of dermis-like tissue rich in blood capillaries. Left untreated, these tumors result in blindness and cases that were treated by surgery, occasionally followed by corneal transplantation, did not result in optimal vision.

Here we report the first evidence of linkage for X-linked CD to Xq24-Xter, telomeric to DXS1001, an interval of 38 CM, in an extended Puerto Rican family.