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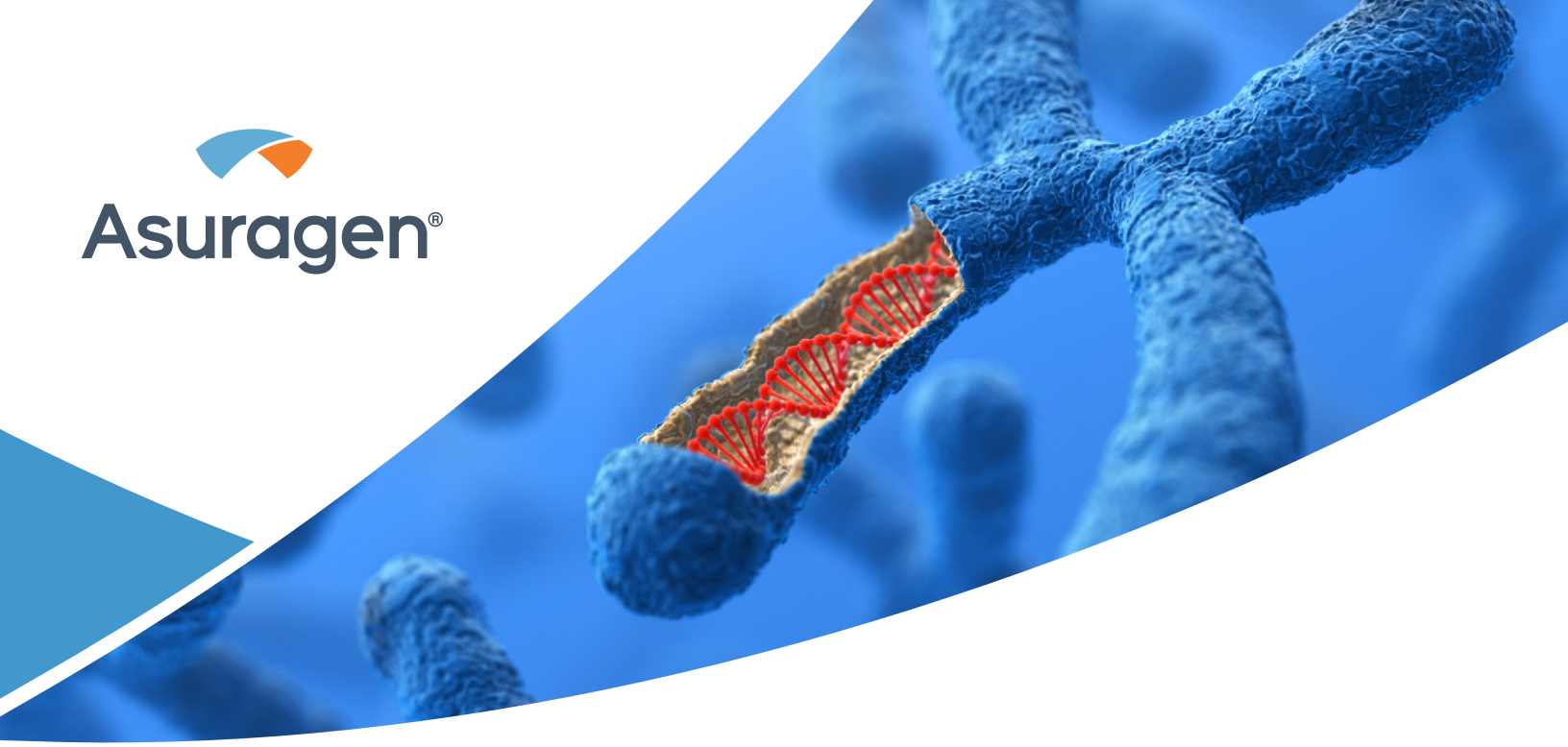

AmplideX®

PUBLICATIONS SYNOPSES

AmplideX® Publications Synopses

NO.	TITLE	AUTHOR	SYNOPSIS	JOURNAL	YEAR
1	A Novel *FMR1* PCR Method for the Low Abundance Expanded Alleles and Full Mutations in Routine Detection of Fragile X Syndrome	Filopovic-Sadic et al.	First publication that establishes the reproducible detection of all expanded alleles up to at least 1300 CGG. Results indicate that the use of this *FMR1* PCR procedure can reduce the burden of Southern blotting by 10-50 fold compared to current testing procedures.	CLIN CHEM	2010
2	An information-Rich CGG Repeat Primed PCR That Detects the Full Range of Fragile X Expanded Alleles and Minimizes the Need for Southern blot Analysis	Chen et al.	Evaluation of a 3-primer CGG repeat-primed *FMR1* PCR with the capability to detect repeat expansions irrespective of size and resolve zygosity in females. Identification of AGG interspersions are also described as a differentiator of this approach.	J MOL DIAGN	2010
3	Fragile X Analysis of 1112 Prenatal Samples From 1991 to 2010	Nolin et al.	Fragile X analysis of 1112 pregnancies identified 558 normal, 106 intermediate, 216 premutation, and 232 full mutation fetuses of 509 maternal, intermediate, and premutation alleles, 350 (68.7%) were unstable on transmission with expansions ranging from one repeat to the full mutation. The smallest premutation alleles expanding to the full mutation were in mothers with 65 and 66 repeats. Transmissions from women with or without a family history of fragile X suggested greater instability in women from families that included full mutation expansions.	PRENAT DIAGN	2011
4	High-Resolution Methylation Polymerase Chain Reaction for Fragile X Analysis: Evidence for Novel *FMR1* Methylation Patterns Undetected in Southern Blot Analyses	Chen et al.	Provides the first published evidence of a robust, semi-quantitative methylation PCR methodology with concordance to Southern blot data across both male and female alleles. Distinct populations of premutation mosaics with skewed methylation were observed in ~80% of female carriers that were masked using SB analysis. Note that the mPCR product configuration was changed from this published format.	GENET MED	2011
5	The Role of AGG interruptions in the Transcription of *FMR1* Premutation Alleles	Yrigollen et al.	Evaluated both the number of AGG interruptions and the resulting length of the uninterrupted 3' CGG repeat length in premutation alleles on two large cohorts of male and female carriers. The findings indicate that neither the number of AGG interruptions, nor their position along the CGG tract have a significant affect on mRNA levels in premutation carriers. Authors also observed a highly significant correlation between CGG repeat number (as both total length and length of pure CGG stretch) and *FMR1* mRNA expression levels, in both males and females. Importantly, they did not observe any significant difference in *FMR1* mRNA levels in premutation carriers based on age.	PLOS ONE	2011
6	Evaluation of the Human Fragile X Mental Retardation 1 Polymerase Chain Reaction Reagents to Amplify the *FMR1* Gene: Testing in a Clinical Diagnostic Laboratory	Nahhas et al.	Multicentre evaluation of AmplideX® *FMR1* PCR using 70 previously characterised clinical specimens. 100% agreement was achieved for all size ranges, including 28 full mutation and 17 premutation samples.	GENET TEST MOL BIOMARKERS	2011
7	Trisomic Pregnancy and intermediate CGG Repeat Length at the *FMR1* Locus	Kline et al.	Clinical research using an early AmplideX® *FMR1* PCR prototype to investigate the association of intermediate maternal repeats with the risk of a trisomy pregnancy. An association was noted, but the odds ratio was <3.	HUM REPROD	2012
8	AGG interruptions Within the Maternal *FMR1* Gene Reduce the Risk of Offspring With Fragile X Syndrome	Yrigollen et al.	The presence of AGG interruptions reduced the risk of transmission of a full mutation for all maternal (premutation) repeat lengths below ~100 CGG repeats, with a differential risk (0 vs. 2 AGG) exceeding 60% for alleles in the 70- to 80-CGG repeat range. Study results underscore the importance of these data in personalizing patient risk in genetic counseling.	GENET MED	2012
9	Performance Evaluation of Two Methods Using Commercially Available Reagents for PCR-Based Detection of *FMR1* Mutation	Juusola et al.	Comparison of Abbott and Asuragen. Asuragen strongly favored based on *FMR1* PCR reagents from 5x to 25x higher sensitivity for premutation and full mutation detection, and 2.5-fold reduced time to result, and superior workflow.	J MOL DIAGN	2012
10	Reliable and Sensitive Detection of Fragile X (Expanded) Alleles in Clinical Prenatal DNA Samples With a Fast Turnaround Time	Seneca et al.	A large set of blinded, previously analyzed prenatal DNA samples evaluated using AmplideX® *FMR1* PCR. This cohort of 67 fetal DNAs contained 18 full mutations (including 1 mosaic), 12 premutations, 9 intermediate, and 28 normal samples (including 3 homozygous female samples). AmplideX® had a 100% specificity and a 97.4% sensitivity in comparison with SB analysis. All homozygous alleles were correctly resolved. The assay was also able to reproducibly detect a 2.5% premutation and a 3% full-mutation mosaicism in a normal male background. Implementation of AmplideX® will significantly reduce reflex testing using SB analyses.	J MOL DIAGN	2012

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11	Prenatal Population Screening for Fragile X Carrier and the Prevalence of Premutation Carriers in Korea	Han et al.	First publication to study the prevalence of FXS permutation carriers and *FMR1* allele distribution in Korean normal pregnant women using the 3-primer AmplideX® *FMR1* PCR kit. This publication supports the use of AmplideX® reagents in an *FMR1* population screening workflow, due to its robust performance, high sensitivity and allele resolution.	J GENET MED	2012
12	*FMR1* CGG Allele Size and Prevelance Ascertained Through Newborn Screening in the United States	Tassone et al.	A US-based pilot newborn screening study for FXS that used AmplideX® PCR methodology for analyzing 14,207 blood spot samples collected since 2008. This publication demonstrates the feasibility of fragile X newborn screening and supports the use of CGG detecting methodology, such as AmplideX®, to identify the full range of *FMR1* genotypes in the general newborn population.	GENOME MED	2012
13	Fragile X AGG Analysis Provides New Risk Predictions for 45-69 Repeat Alleles	Nolin et al.	Authors using Xpansion Interpreter™ investigated the effect of AGG interruptions on fragile X repeat instability upon transmission of fragile X alleles with 45–69 CGG repeats, including 375 mothers, 48 fathers, and 538 offspring (457 maternal and 81 paternal transmissions). The number of AGG interruptions and the length of uninterrupted CGG repeats at the 3' end were correlated with repeat instability on transmission. Maternal alleles with no AGGs conferred the greatest risk for unstable transmissions. The magnitude of repeat expansion was larger for alleles lacking AGG interruptions. Transmissions from paternal alleles with no AGGs also exhibited greater instability than those with one or more AGGs. Characterization of the AGG structure within the *FMR1* repeat allows more accurate risk estimates of repeat instability and expansion to full mutations with important implications for patient counseling.	AM J MED GENET A	2013
14	Population-Based Estimates of the Prevalence of *FMR1* Expansion Mutations in Women With Early Menopause and Primary Ovarian Sufficiency	Murray et al.	This study aimed to estimate the prevalance of mutation in Primary Ovarian Insufficiency (POI) and early menopause. The prevalance of the premutation was 2% in POI and 0.7% in menopause compared to 0.4% in controls. The intermediate alleles were not significant risk factors for either early menopause or POI. *FMR1* premutations are not as prevalent in women with ovarian insufficiency as previous estimates have suggested, but they still represent a substantial cause of primary ovarian insufficiency and early menopause.	GENET MED	2013
15	Frequency of *FMR1* Premutation Carriers and Rate of Expansion to Full Mutation in a Retrospective Diagnostic *FMR1* Korean Sample	Jang et al.	A retrospective study on the prevalence of *FMR1* premutation carriers in a large (10,241 sample) cohort of Korean pre-conceptional and pregnant women. The study uses AmplideX® to track the frequency of permutations and the rate of expansion to full mutation in carrier offsprings.	CLIN GEN	2013
16	Maternal *FMR1* Premutation Allele Expansion and Contraction in Fraternal Twins	Alfaro et al.	A report of a maternal *FMR1* premutation allele that underwent both expansion into full mutation and a large (39 repeat) contraction into the gray zone within a single pregnancy of fraternal twins. *FMR1* evaluation was carried out using AmplideX® *FMR1* PCR.	AM J MED GENET PART A	2013
17	Transmission of an *FMR1* Premutation Allele in a Large Family Identified Through Newborn Screening: the Role Off AGG interruptions	Yrigollen et al.	Used AmplideX® PCR to trace the molecular structure (AGG interruptions) and the transmission of an *FMR1* premutation allele in a multigenerational family. Transmission of the premutation allele was traced through five generations in 14 of the 23 individuals with minimal expansion. Premutation stability was attributed to the presence of two stabilizing AGG interruptions.	J HUM GENET	2013
18	A Novel Methylation PCR That Offers Standardized Determination of *FMR1* Methylation and CGG Repeat Length Without Southern Blot Analysis	Grasso et al.	Authors from two European laboratories report the first independent validation of mPCR for the analysis of CGG repeat length and methylation status without Southern blot analysis. Results from 76 residual samples were 99% concordant with Southern blot and included comparisons with novel sample types and sex chromosome aneuploidies that might be encountered in routine clinical testing.	J MOL DIAGN	2013
19	A Novel Deletion to Normal Size in the Sperm of a Fragile X Full Mutation Male	Duan et al.	This study reports first case of deletion in the sperm of the fragile X full mutation male. The full mutation was present in both blood and buccal swab but was absent in sperm. Further analysis indicated that the loss of AGG interruptions may associate with germline instability.	CLIN GENET	2014

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20	Impaired Response Inhibition is Associated With Self-Reported Symptoms of Depression, Anxiety, and ADHD in Female *FMR1* Premutation Carriers	Kraan et al.	In this study, 35 female PM were matched with 35 control females and tested for executive function. Compared to controls, PM carriers were significantly elevated on self-reported social anxiety and ADHD-PI symptoms. Irrespective of mental symptoms, female PM carriers performed significantly worse than controls on a response inhibition test: significant correlations between executive function performance and self-reported symptoms of anxiety, depression and ADHD-PI where noted.	AMERICAN JOURNAL OF MEDICAL GENETICS	2013
21	Molecular Cytogenetic Analysis of Xq Critical Regions in Premature Ovarian Failure	Beke et al.	The authors performed *FMR1* gene analysis using Southern blot and AmplideX® PCR to identify the relationship between *FMR1* premutation status and the premature ovarian failure disease on the patient in this case study. They conclude for this case study that the karyotyping is definitely helpful in the evaluation of premature ovarian failure patients, to identify the non-submicroscopic chromosomal rearrangement, and the array CGH technique can be used for most efficient detection and mapping of exact deletion breakpoints of the deleted Xq region.	MOLECULAR CYTOGENETICS	2013
22	Intermediate CGG Repeat Length at the *FMR1* Locus Is Not Associated With Hormonal indicators of Ovarian Age	Kline et al.	In a detailed retrospective population study of 1000 samples, the authors found no link between CGG repeat length, X-activation or AGG status and the hormones AMH and FSH within intermediate alleles. *FMR1* alleles in the 35-58 CGG repeat range do not appear to influence hormonal indicators of ovarian age.	MENOPAUSE	2014
23	CGG Allele Size Somatic Mosaicism and Methylation in *FMR1* Premutation Alleles	Pretto	The authors found that CGG repeat numbers correlate well with % methylation and mRNA expression levels. Inter and intra tissue somatic instability and differences in % methylation were observed between blood and fibroblast (n=4) and also between blood and different brain regions (n=3).	JOURNAL OF MEDICAL GENETICS	2014
24	Fragile X Syndrome Screening in Chinese Children with Unknown Intellectual Developmental Disorder	Chen et al.	553 patients between 6 months to 18 years with unknown moderate to severe IDD were recruited from two children's hospitals. The size of the CGG repeat was identified using a AmplideX® *FMR1* PCR assay. Five full mutations were identified (1 familial and 4 sporadic IDD patients), and size mosaicism was apparent in 4 of these FXS patients (4/5 = 80%). The influence of AGG interruptions on the CGG expansion during maternal transmission was analyzed in 24 mother-son pairs (10 pairs with 1 AGG and 14 pairs with 2 AGGs). AmplideX® *FMR1* PCR assay generates reliable and sensitive results across a large number of patient specimens, and is suitable for clinical genetic diagnosis. Using this assay, the prevalence of FXS was 0.93% in Chinese children with unknown IDD.	BMC PEDIATR	2015
25	Fragile X Full Mutation Expansions are Inhibited by One or More AGG Interruptions in Premutation Carriers	Nolin et al.	This publication analyzed 1040 alleles from 705 families and examined transmissions from maternal and paternal alleles with 45-90 repeats. AmplideX® PCR was used for CGG sizing and Asuragen's CLIA lab determined the AGG pattern in each sample. The study strengthened the association of AGG repeats with CGG repeat stability and provided more accurate risk estimates of full mutation expansions for women with 45-90 repeat alleles.	GENET MED	2015
26	AGG Interruptions and Maternal Age Affect *FMR1* CGG Repeat Allele Stability During Transmission	Yrigollen et al.	The study assessed the outcomes of 108 intermediate and 710 premutation alleles that were transmitted from parent to child, and collected from four international clinical sites. The results were used to revise our initial model that predicted the risk of a maternal premutation allele expanding to a full mutation during transmission and to test the effect of AGG interruptions on the magnitude of expanded allele instability of intermediate or premutation alleles that did not expand to a full mutation.	J NEURODEV DISORD	2015

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