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Multiprobe FISH method for enhanced detection of chromosome 9 heterochromatin rearrangements

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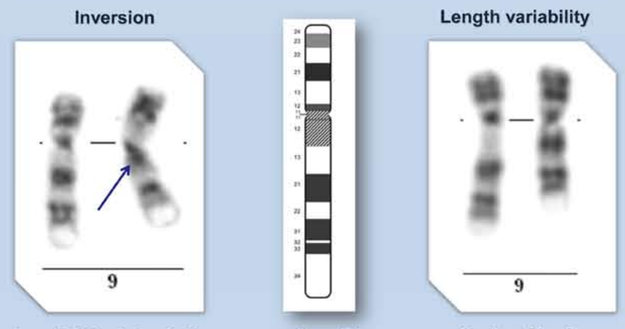
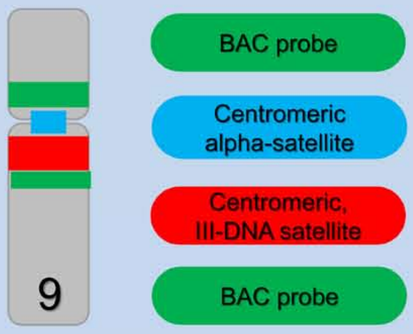
Introduction:
Heterochromatin rearrangements are believed to be clinically insignificant variants of the human karyotype. However, several authors have studied the possible association of heterochromatin variants with certain clinical diagnoses, especially with reproductive failure. Variants of heterochromatin area of chromosome 9 are the most common. They involve enlargement (qh+) or shortening (qh-) of the heterochromatin block as well as the pericentric inversion - inv(9)(p12q13). More complex variants of this area may include duplication and/or combination of above mentioned rearrangements.
Distinguishing between benign and pathological rearrangement in this area can be challenging. The classical G and/or C-banding are not very specific and array methods like SNP-array/array-CGH are usually not able to analyze precisely this pericentric region, which is composed mainly of satellite DNA.

Chromosome 9 variants



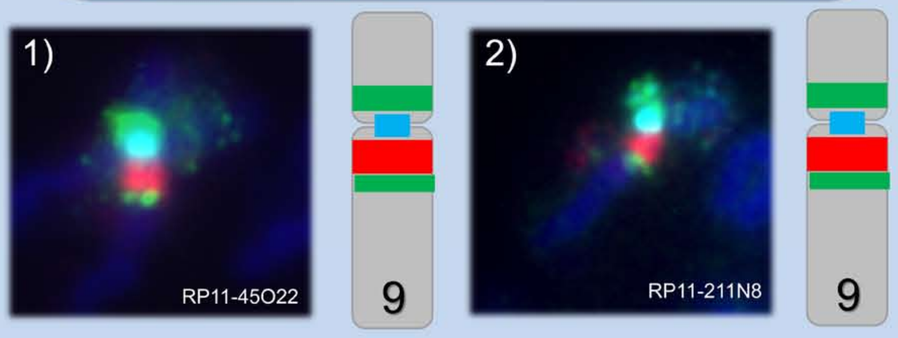
inv(9)(p12q13) chr. 9 9qh+/9qh-

FISH probes legend

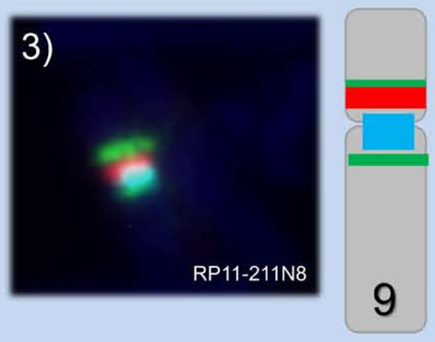


Methods:
For enhanced analysis of heterochromatin area of chromosome 9 we implemented a special molecular cytogenetic method using three different FISH probes - centromeric alpha-satellite, centromeric III-DNA satellite and a specific BAC probe (hybridizing on 9p11/9p12 and 9q13 homologous sequences – the particular clone is specified).

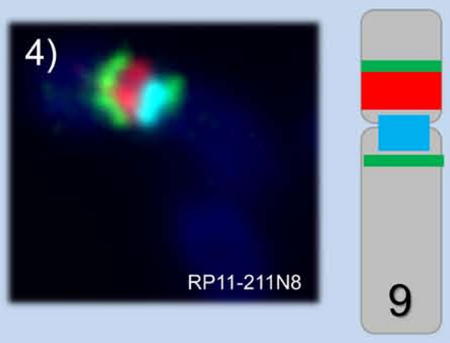
Results:
The outcomes of this examination in 20 patients with different clinical indications are demonstrated.



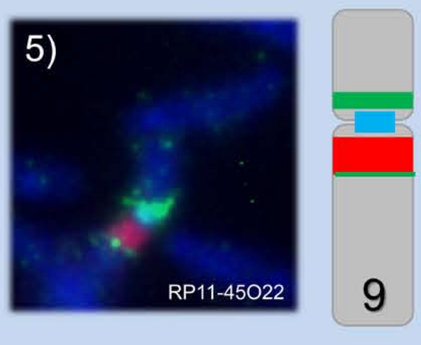
Control: Male (43 years), healthy
46,XY (normal chromosome 9)



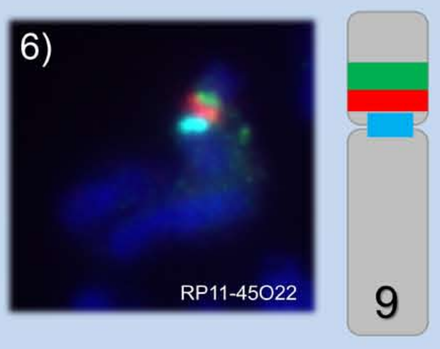
Female (32 years), healthy
46,XX,inv(9)(p12q13)



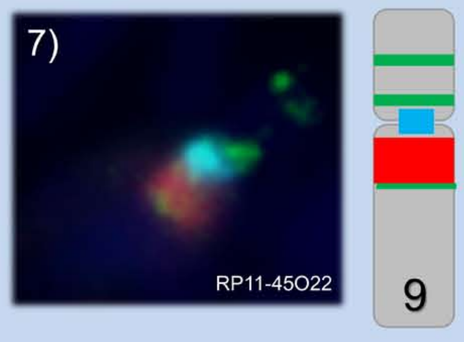
Male (32 years), sterility
46,XY,inv(9)(p12q13)



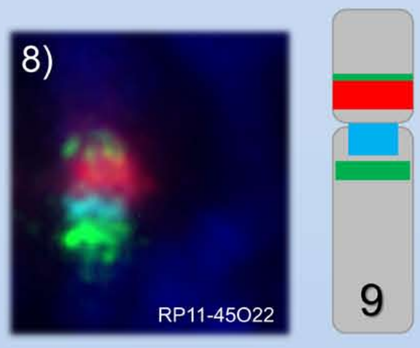
Male (36 years), sterility
46,XY,inv(9)(q21.2q34.2)



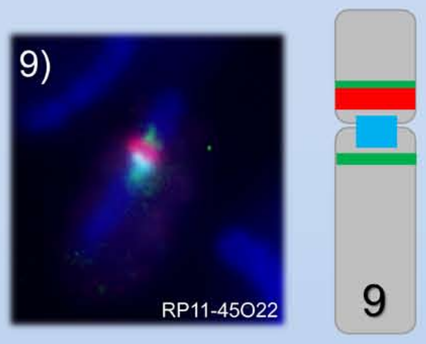
Male (2 years), epilepsy, mental retardation, micropenis
46,XY,inv(9)(p12q21)



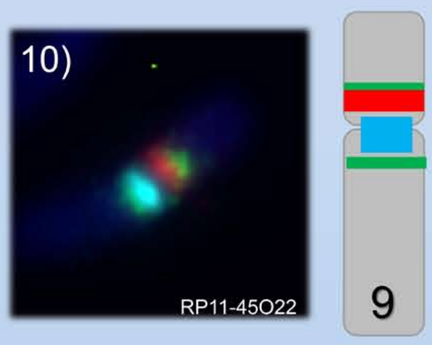
Male (1 year), dysmorphy, psychomotor retardation
47,XYY,inv(9)(p12p24)



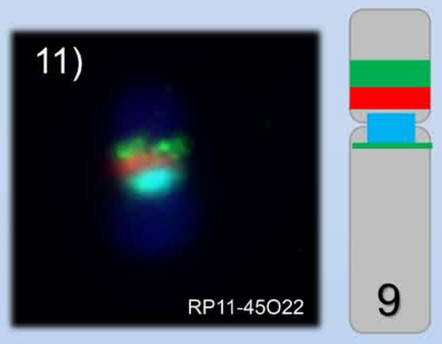
Female (33 years), sterility
46,XX,inv(9)(p12q13), t(15;22)(q26.1;p12)



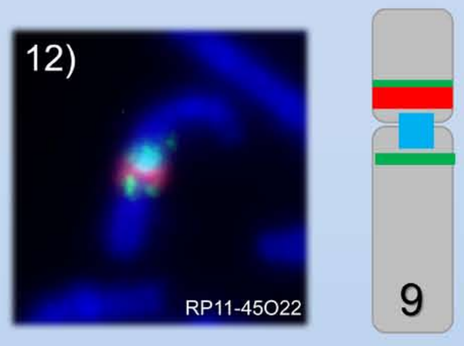
Female (56 years), healthy, mother of individual nr. 8
46,XX,inv(9)(p12q13)



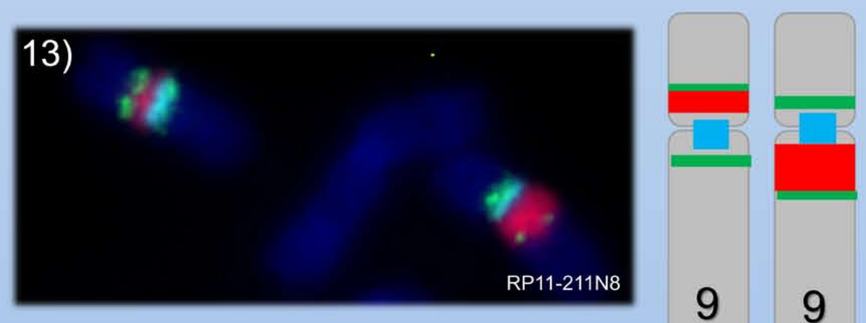
Male (42 years), sterility
46,XY,inv(9)(p12q13)



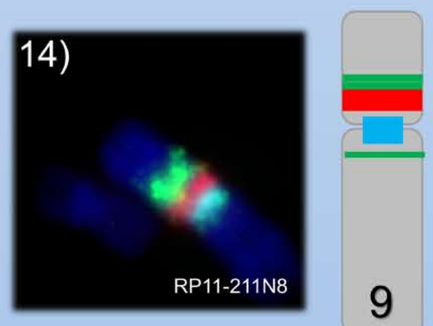
Female (28 years), sterility
46,XX,inv(9)(p12q13)



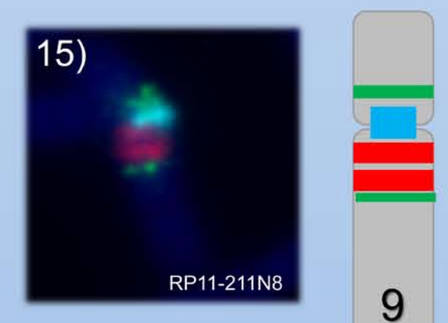
Female (28 years), sterility,
46,XX,inv(9)(p12q13)



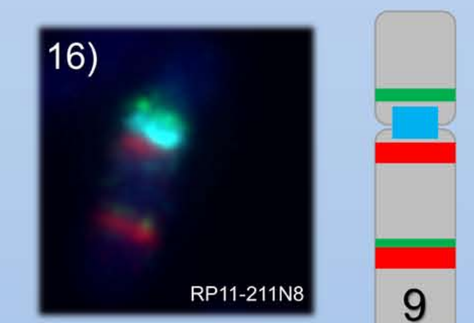
Female (25 years), gamete donor
46,XX,9qh+,inv(9)(p12q13)



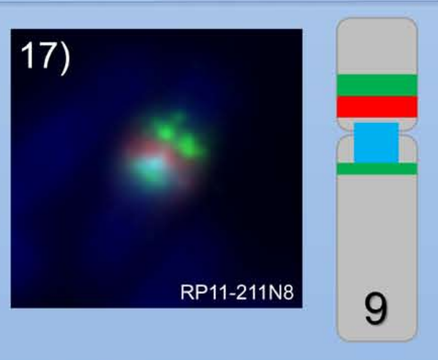
Female (26 years), gamete donor
46,XX,der(9)dup(9)(p11.2p12) inv(9)(p12q13)



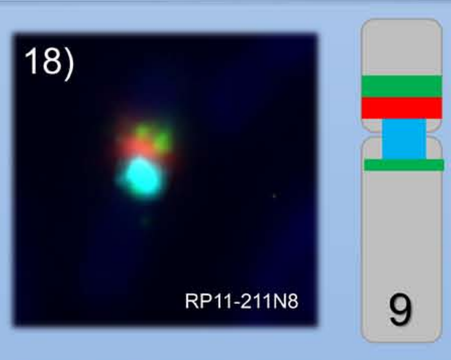
Female (28 years), gamete donor
46,XX,der(9)dup(9)(q12q13)



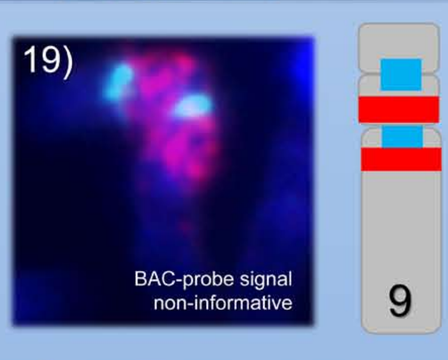
Female (34 years), sterility
46,XX,inv(9)(q12q31.1)



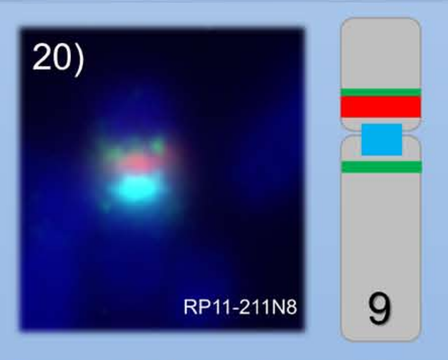
Female (34 years), gamete donor
46,XX,inv(9)(p12q13)



Female (2 years), small stature
46,XX,inv(9)(p12q13)



Fetus (16 weeks), healthy
46,XY,dic(9)(pter->q13::p12->qter)



Female (36 years), gravidity mother of individual nr. 19
46,XX,inv(9)(p12q13)

Conclusion: Multiprobe FISH method is an useful tool for detailed analysis of chromosome 9 variants and rearrangements.

References:
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This study was supported by the GAUK 523456 grant project.