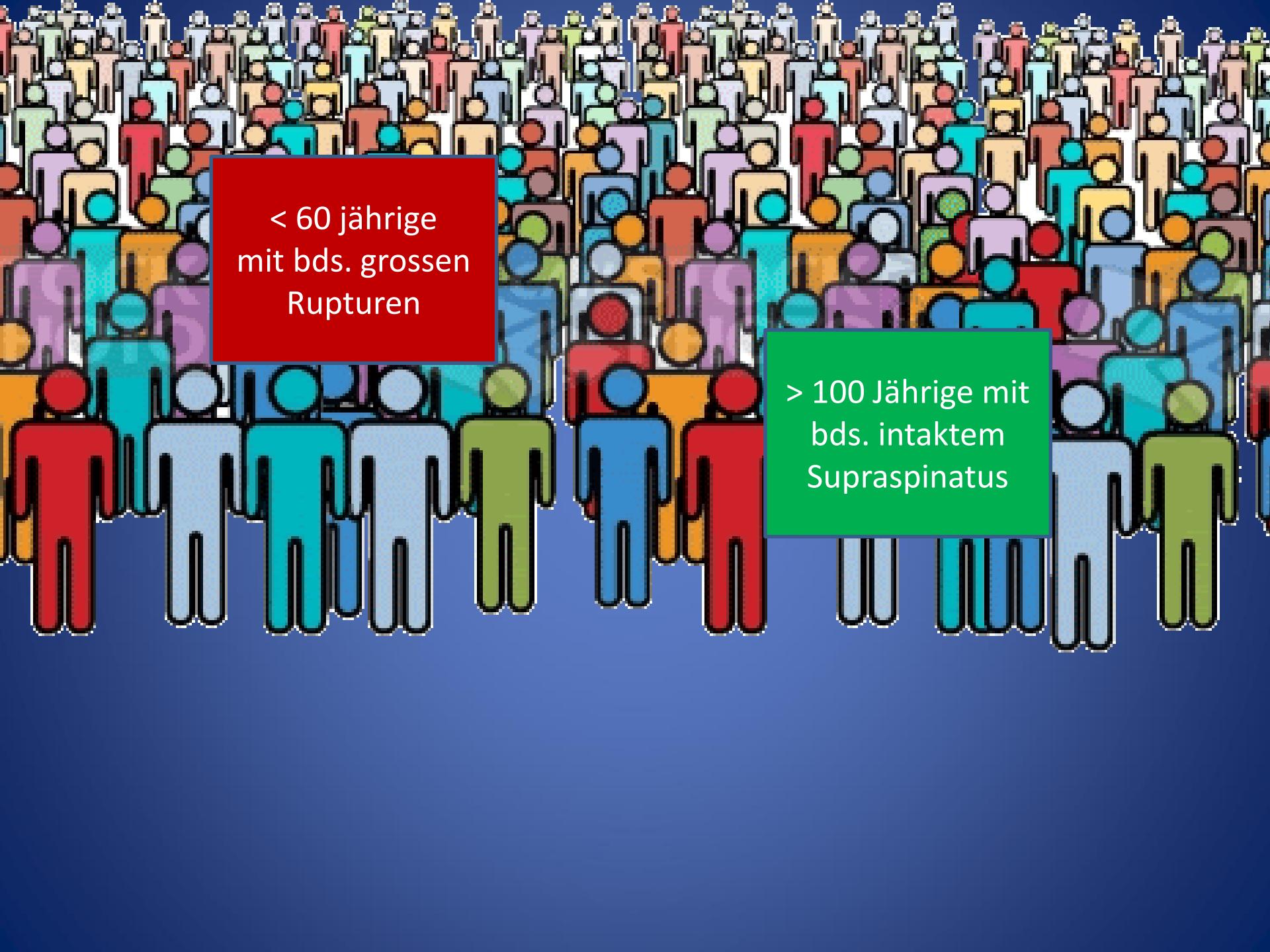


Candidate Gene Approach Identifies Six SNPs in Tenascin-C (TNC) Associated With Degenerative Rotator Cuff Tears

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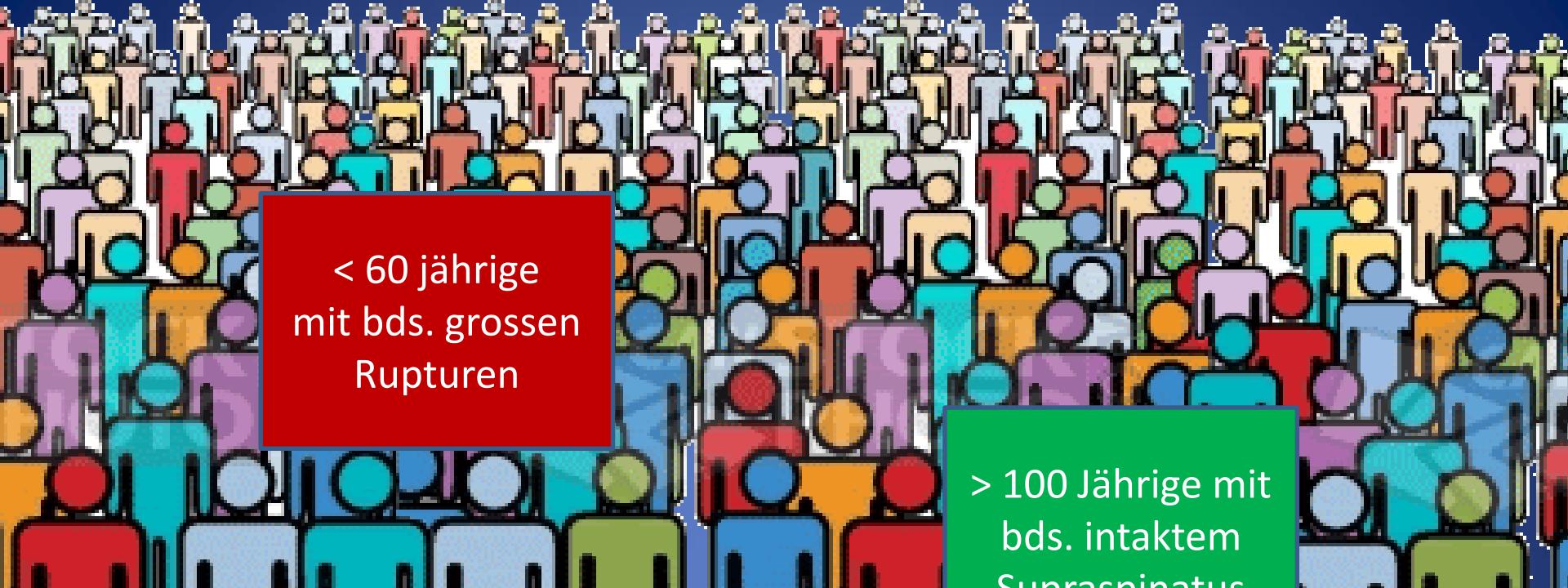
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A large crowd of colorful human icons (red, blue, green, yellow, purple) is positioned against a blue gradient background. Two text boxes are overlaid on the crowd: a red box on the left and a green box on the right.

< 60 jährige
mit bds. grossen
Rupturen

> 100 Jährige mit
bds. intaktem
Supraspinatus



< 60 jährige
mit bds. grossen
Rupturen

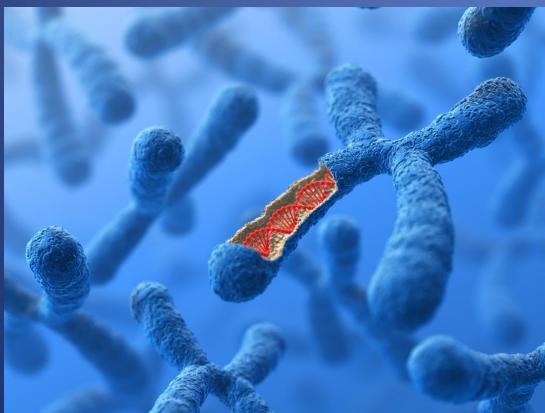


> 100 Jährige mit
bds. intaktem
Supraspinatus



Hintergrund

Full-Thickness Tear



Ursachen der ErstRuptur anno 2009

Trauma (Codman 1911)

Alter (Codman 1911)

Überlastung (Codman 1911)

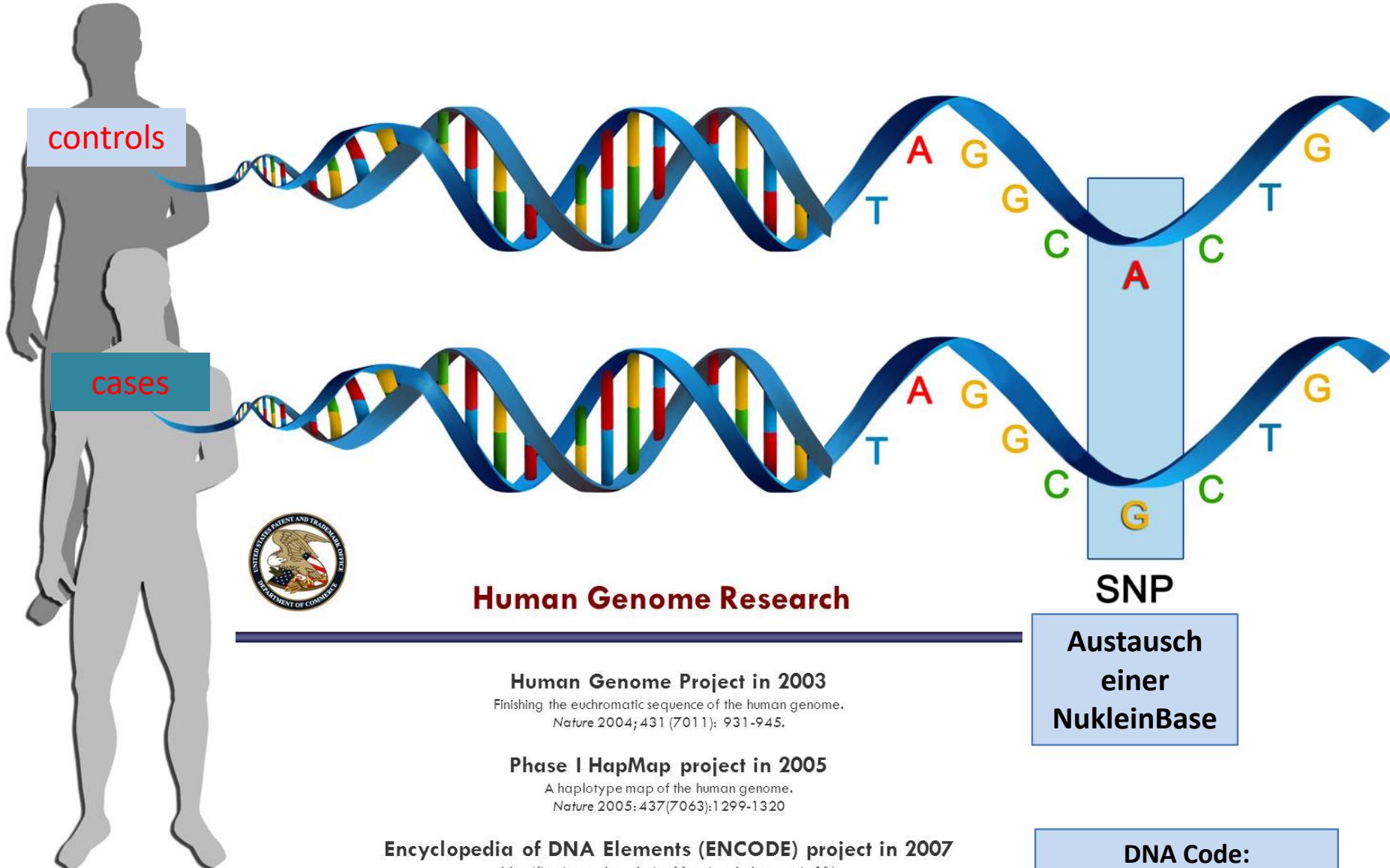
atraumatisch (Codman 1931)

subakromiale Enge (Neer 1972)

familiäre Häufung (Harvie 2004, Tashjian 2009)

Nikotin (Baumgarten 2010)

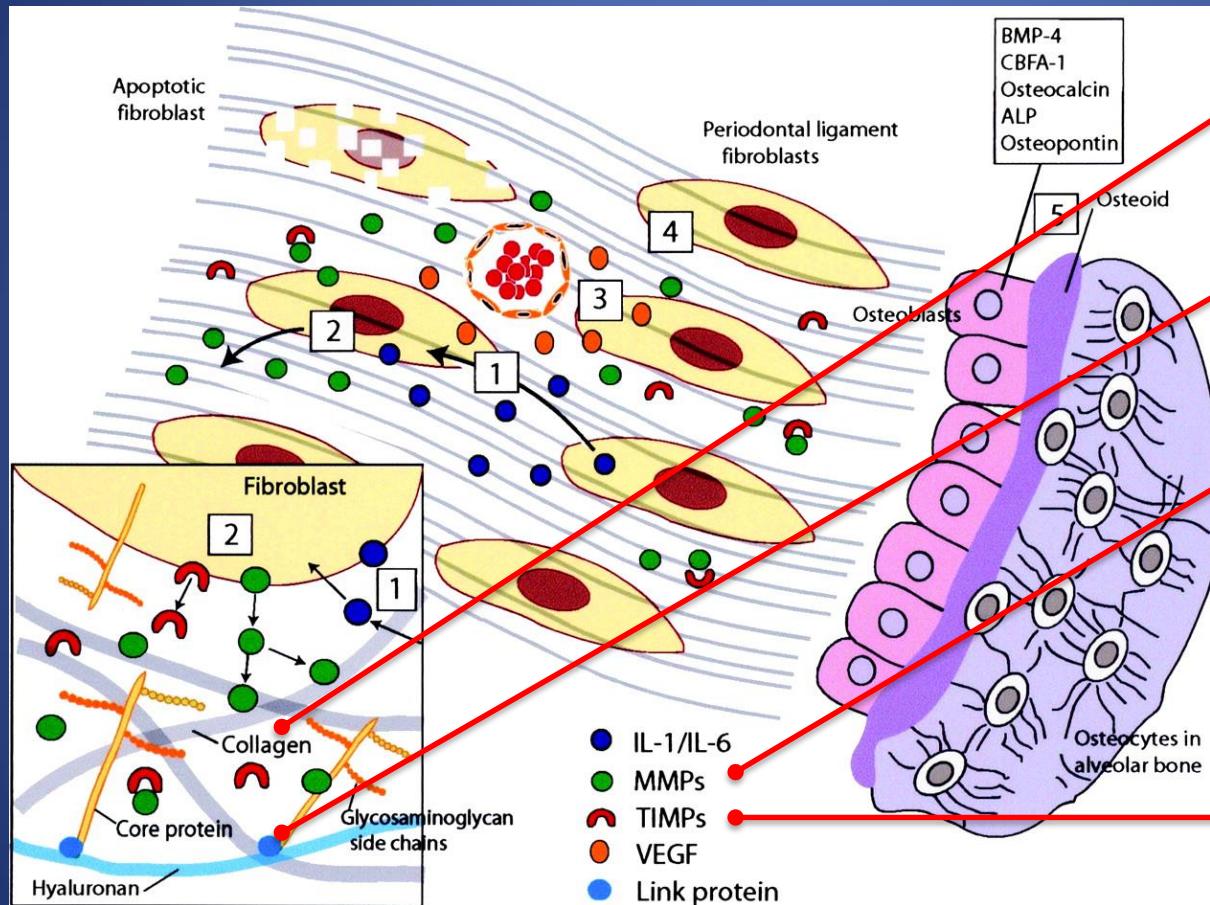
Assoziation mit erblichen Faktoren?



**DNA Code:
10 Mio Loci
genetischer Varianz**

**1% der SNPs
exonisch**

Fokus: DNA Abschnitte die für Sehnenheilungsproteine codieren.



8 Kandidatengene /

1. Schritt: an 79 proteincodierenden SNPs die Genotyp und Allelefrequenz bestimmt.

59 Patienten
bds. degenerative
SS+IS Ruptur,
Nichtraucher;
Ø Alter 71a

32 Kontrollen
beidseits intakte
Rotatorenmanschette,
Nichtraucher;
Ø Alter 87a

2 SNPs im TNC Gen im LD

Gene [¶]	SNP [¶]	HWE.all [¶]	HWE.contr [¶]	HWE.rupt [¶]	RvsC.Gt [¶]	RvsC.allelest [¶]
TNC [¶]	rs5900112 [¶]	0.775 [¶]	1.000 [¶]	0.447 [¶]	0.106 [¶]	0.081 [¶]
TNC [¶]	rs13321 [¶]	1.000 [¶]	1.000 [¶]	0.577 [¶]	0.053 [¶]	0.030[¶]
TNC [¶]	rs2104772 [¶]	0.678 [¶]	0.726 [¶]	0.297 [¶]	0.416 [¶]	0.753 [¶]
TNC [¶]	rs1138545 [¶]	0.470 [¶]	0.304 [¶]	0.008[¶]	0.040[¶]	0.550 [¶]
TNC [¶]	rs1061494 [¶]	0.091 [¶]	0.178 [¶]	0.299 [¶]	0.915 [¶]	0.756 [¶]
TNC [¶]	rs1757095 [¶]	0.607 [¶]	1.000 [¶]	0.609 [¶]	0.848 [¶]	0.580 [¶]

[¶]

Sequenzieren von 67010 bp des TNC Gens (142 SNPs)

59 Patienten
beidseits grosse
Sehnenruptur,
Nichtraucher;
mean age 71

32 Kontrollen
beidseits intakte
Rotatorenmanschette,
Nichtraucher;
mean age 87

Erstes Kollektiv: 15 SNPs im LD

3. Schritt: Genanalyse von 67010 bp des TNC Gens (142 SNPs)

59 Patienten

+ 96 Patienten
bds. degenerative
SS+IS Ruptur
Nichtraucher;
Ø Alter 67a

32 Kontrollen

+ 44 Kontrollen
beidseits intakte
Rotatorenmanschette,
Nichtraucher;
Ø Alter 87a

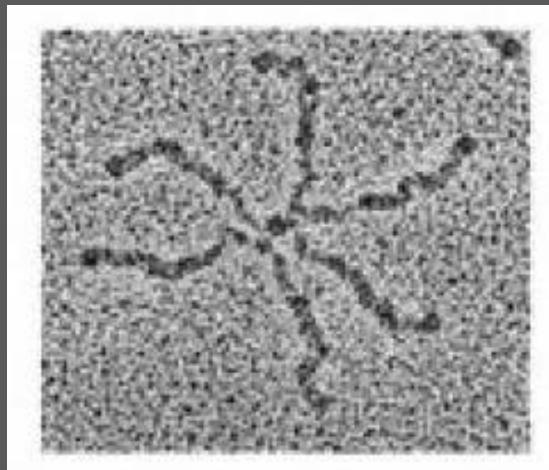
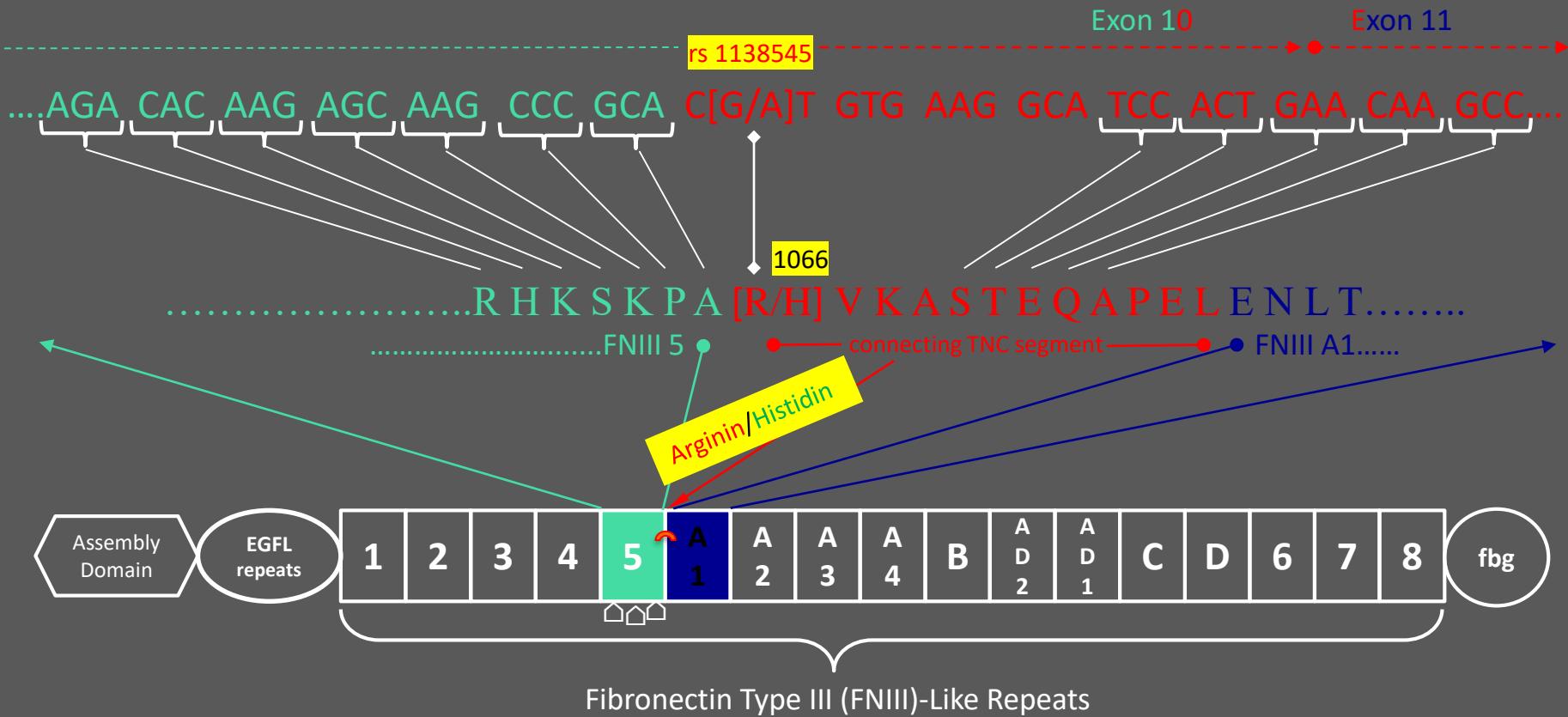
+ Erweiterung um ein
unabhängiges Kollektiv

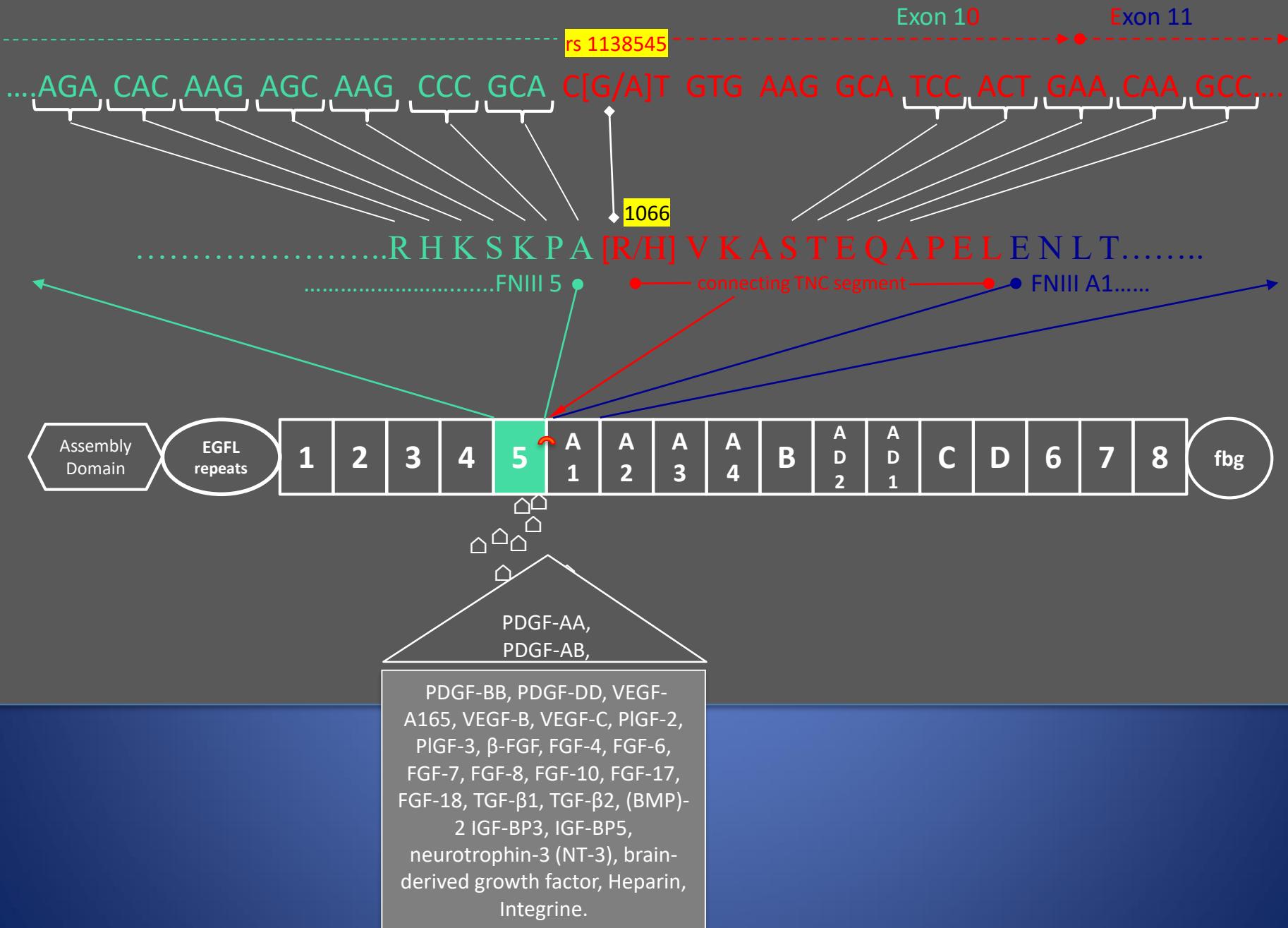
GesamtKollektiv: 6 Treffer

TNC	Controls	Cases	p-Values
rs1138545			
n	75	155	
G/G	0.573	0.759	0.001*
G/A	0.427	0.197	
A/A	0.000	0.044	
minor A	0.213	0.142	0.062
HWE	0.033	0.016	

rs 1138545 (missense Mutation im Exon10)







Konklusion

TNC	Controls	Cases	p-Values
rs1138545			
n	75	155	
G/G	0.573	0.759	0.001*
G/A	0.427	0.197	
A/A	0.000	0.044	
minor A	0.213	0.142	0.062
HWE	0.033	0.016	



Homozygotie am exonischen (TNC) SNP rs 1138545 ist mit degenerativen Rupturen der Supra / Infraspinatussehne assoziiert ($p < 0.001$)

Kluger R, Burgstaller J, Vogl C, Brem G, Skultety M, Müller S. A candidate gene approach identifies six SNPs in Tenascin-C (TNC) associated with degenerative rotator cuff tears. J Orthop Res. 2017 Apr;35(4):894-901.