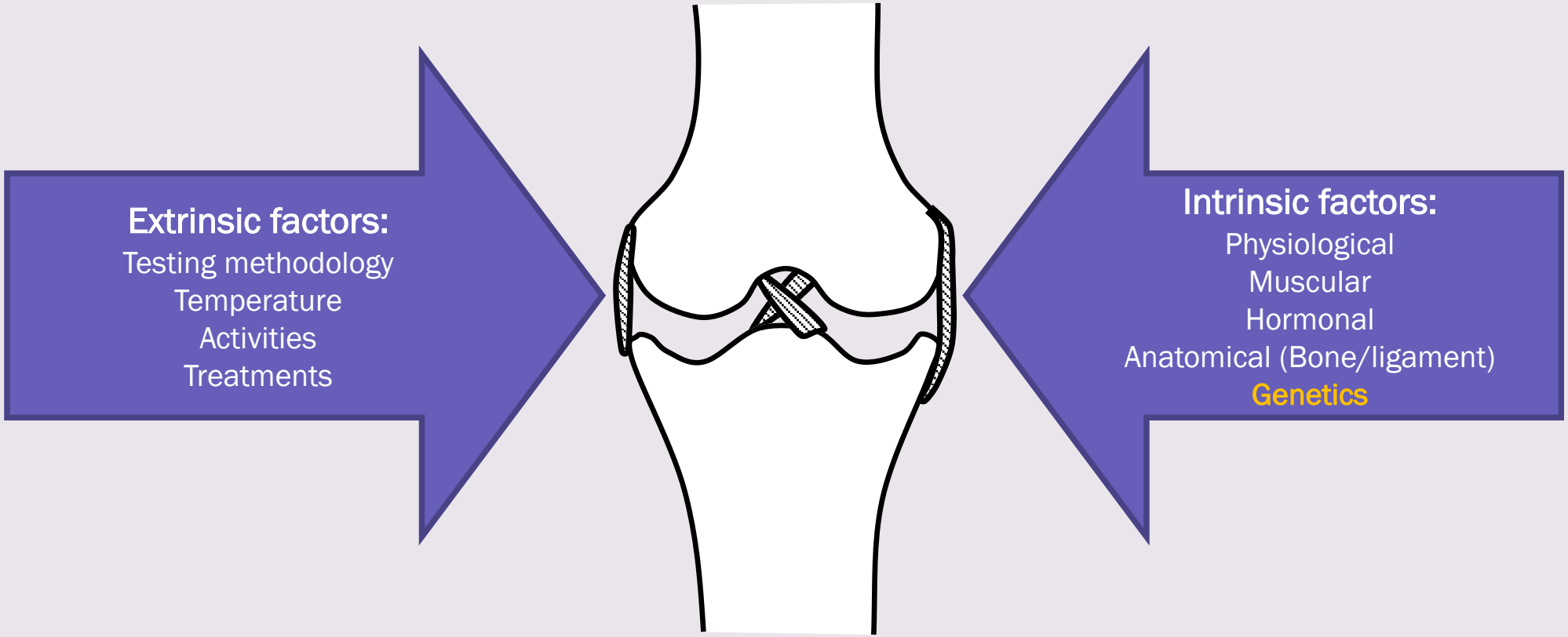
EXPLORING THE ASSOCIATION OF *COL12A1, COL27A1* AND *TNC* VARIANTS WITH KNEE LAXITY

S Beckley, T Branch, R Dey, M Posthumus, AV September & M Collins

Normal knee laxity is a multifactorial phenotype



Bell et al., 2012; Beckley et al., 2022; Beckley et al., 2022; Bulbul et al., 2023

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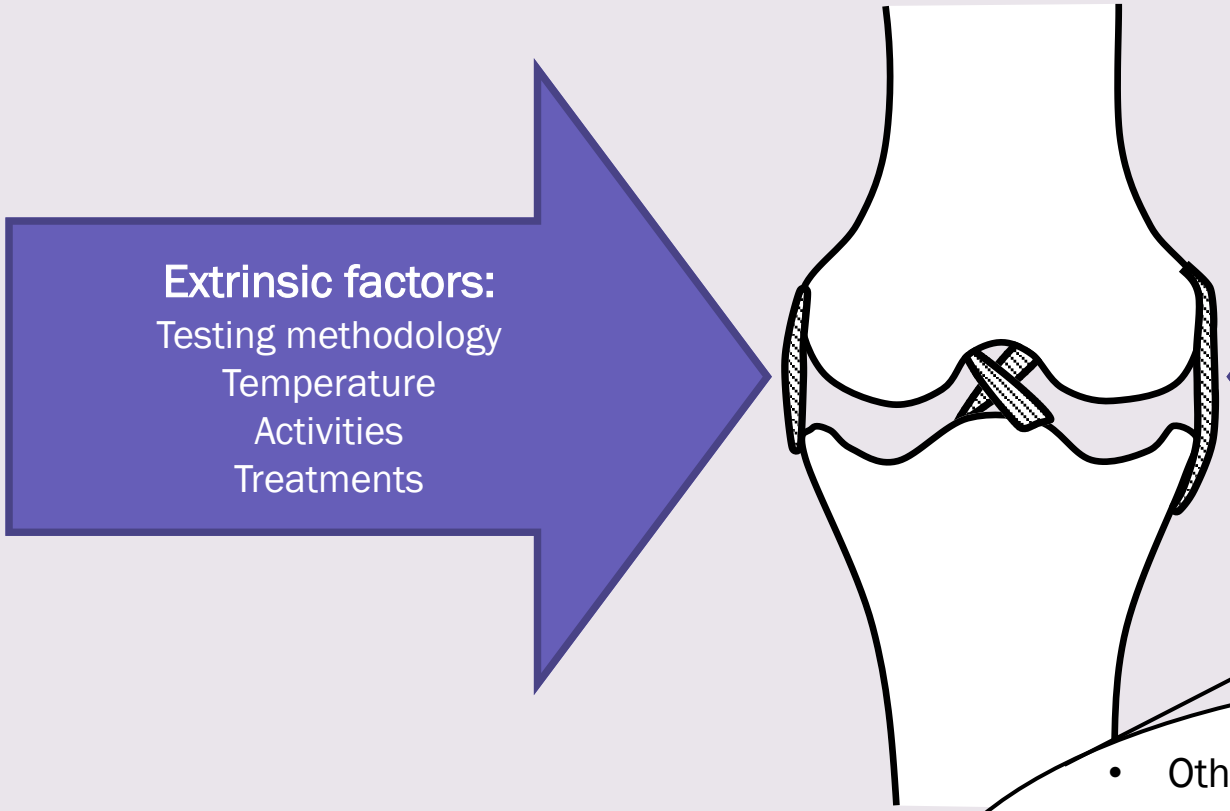


Extrinsic factors:
Testing methodology
Temperature
Activities
Treatments

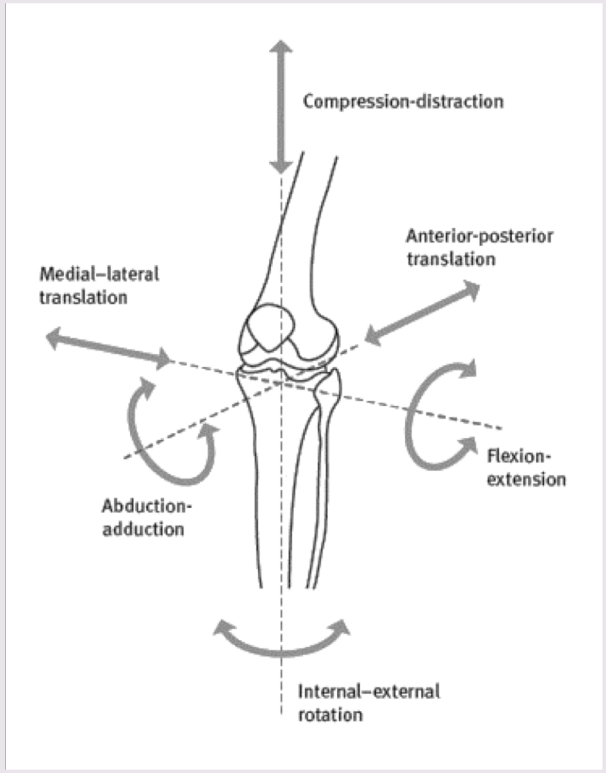
Intrinsic factors:
Physiological
Muscular
Hormonal
Anatomical (Bone/ligament)
Genetics

- Other collagen encoding genes associated with musculoskeletal soft tissue injuries have been associated with knee laxity
- Type XII & type XXVII collagen as well as Tenascin C encoding genes have been associated with risk of Achilles tendinopathy & ACL injuries

Bell et al., 2012; Beckley et al., 2022; Beckley et al., 2022; Bulbul et al., 2023

Aim of the study

Investigate whether types XII (*COL12A1* rs970547) and XXVII (*COL27A1* rs2567706, rs2241671 & rs2567705) collagen, or the Tenascin C (*TNC* rs1061494, rs2104772 & rs1138545) encoding genes are associated with the knee laxity measurements and computed knee ligament (ACL, PCL, MCL, LCL) length changes in the non-dominant and dominant legs.



Shenoy et al. (2013)

Methods

Participants:
n=114

- Moderately active
- Apparently healthy
- Used uninjured knee data
- Self-reported European ancestry
- Consented
- Completed questionnaires
- Blood Donation

Knee laxity measurements

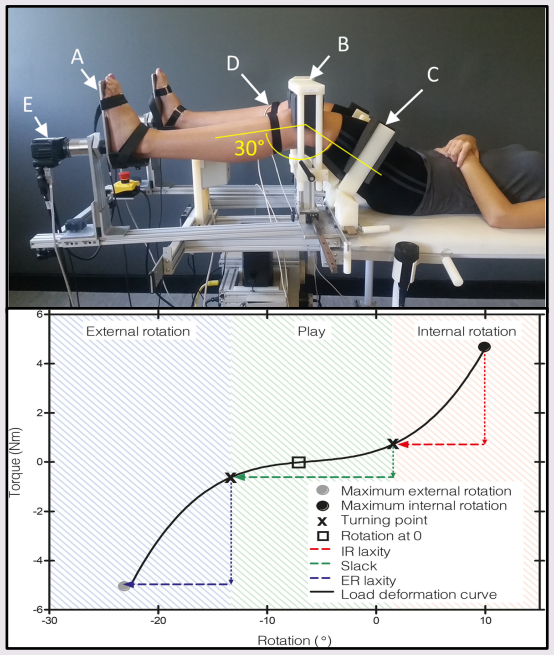
Knee Hyperextension:
Goniometer

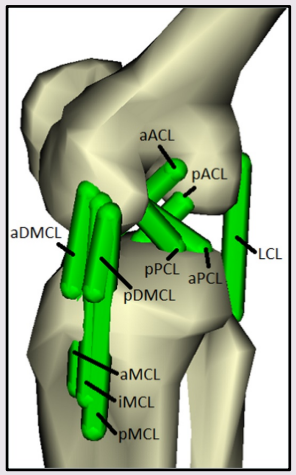
Anterior-posterior knee laxity:
KT-1000

External-internal rotational knee laxity:
RKT device

Input RKT motion data into knee model to calculate difference btw min. & max. length of ACL, PCL, MCL and LCL bundles

Sex (% male)	56.6
Age (years)	26.0 (24.0; 30.0)
Height (cm)	175.0 (167.2; 182.0)
Body mass (kg)	73.7 (61.2; 80.8)
BMI (kg/m^2)	23.7 (21.6; 25.5)
Dominant Leg (% Right)	85.8

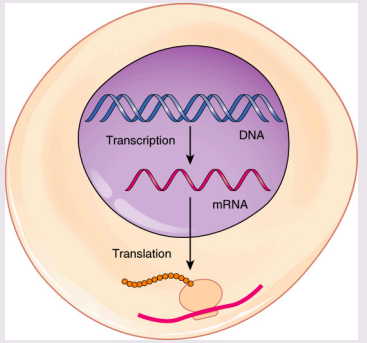




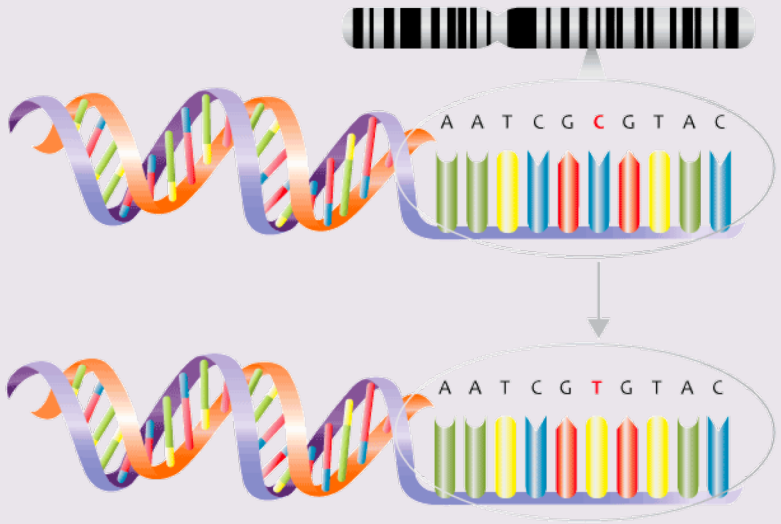
Beckley et al., 2020; Xu et al., 2015

Genetic Concepts

- **Gene**: considered to be basic unit of inheritance. Most genes code for specific proteins, or segments of proteins. Eg. *COL12A1* encodes a chain of Type XII Collagen.



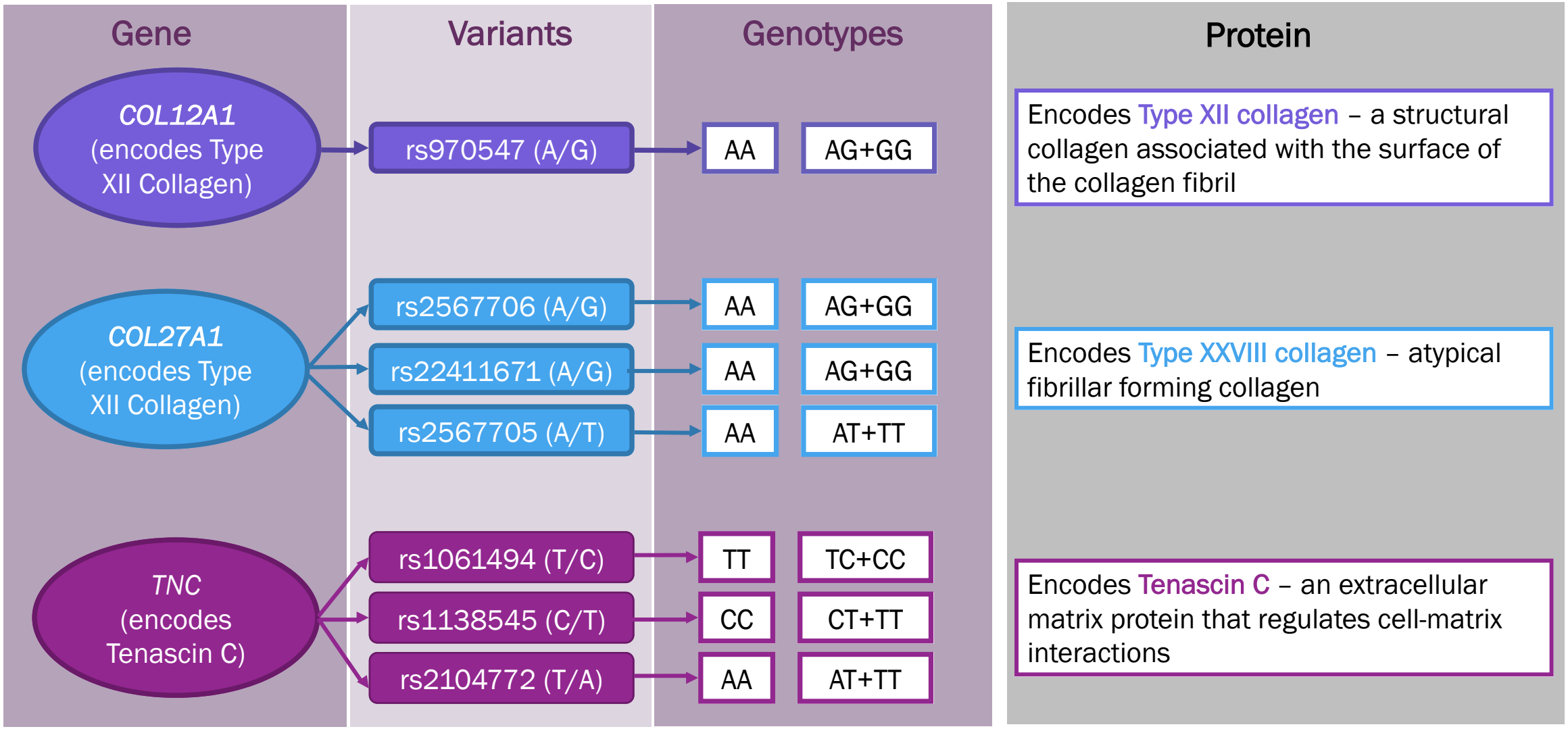
- **Variant (SNP):** variation at a single position in a DNA sequence among individuals.



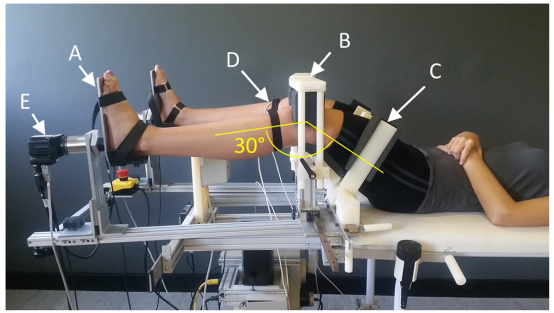
- **Allele**: different versions of the same variant. Eg. C or T

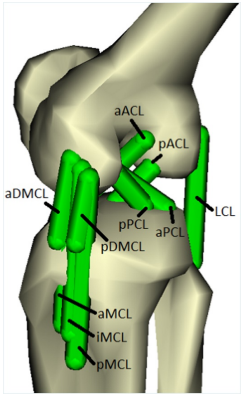
- **Genotype**: allele inherited at a specific locus. Eg. CC, CT or TT

Gene variants of Interest



FINDING: *COL12A1* and *TNC* variants were associated with larger rotation measurements and/or ligament length changes





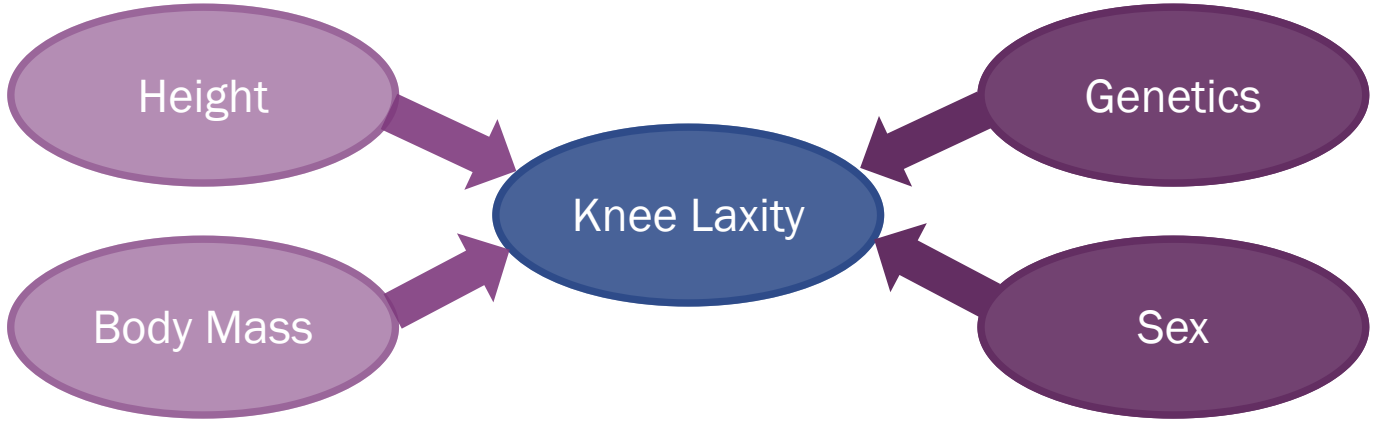
	COL12A1 rs970547	*TNC* rs1061494	
	Dominant Leg		Non-Dominant Leg
External Laxity		CT & CC (C allele)	
Internal Laxity		CT & CC (C allele)	
Slack		CT & CC (C allele)	CT & CC (C allele)
MCL	AG & GG (G allele)	CT & CC (C allele)	
LCL		CT & CC (C allele)	
PCL		CT & CC (C allele)	

= associated with larger measurements

Multiple regression model: *TNC* variants and physical characteristics predicted external rotation, internal rotation & slack measurements in the dominant leg

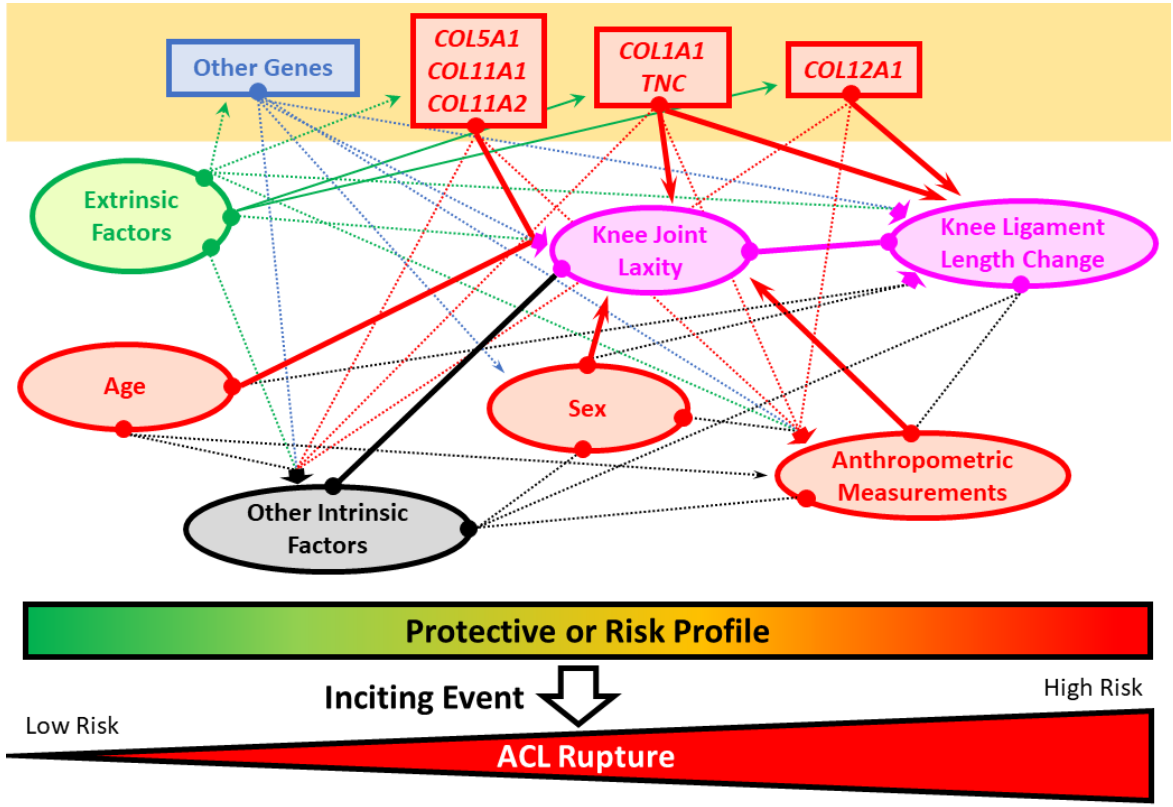
	Sex (female)	Height (cm)	Body Mass (kg)	*TNC* rs1061494 (C allele)
	Dominant Leg			
External Laxity	1.27			1.51
Internal Laxity	0.78	0.05	-0.03	0.93
Slack	3.10			3.52

= positive correlation = negative correlation



Conclusions

- Variants in *COL12A1* & *TNC* may play a role in regulating normal knee laxity
- Other factors such as sex, height and body mass also impact laxity
- Complex interactions exist between genetic variants and intrinsic and extrinsic factors and to modulating knee laxity
- Highlights potential mechanism these variants may influence risk of injury



Acknowledgements

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Ermi

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Health Through Physical Activity, Lifestyle, and Sport RESEARCH CENTRE

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