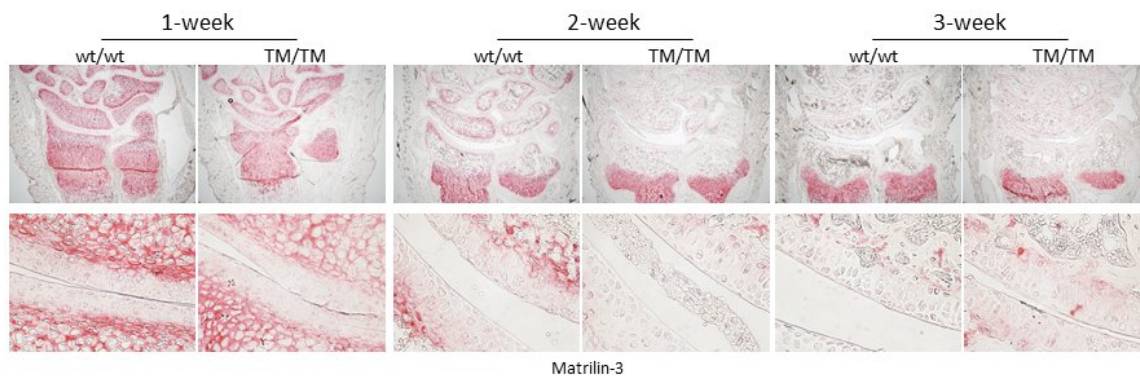




D4.9 partner [UKK]

11/09/2018 Mr Patrick Seifer

Forepaws of wt and matn3 T298M mutant were stained via IHC (Fast Red). Age 1-, 2- and 3-weeks old animals. Decreased Matn-3 Signal in 1-week old mutant mice. No Matn-3 signal in the articular cartilage of 2-weeks old mutant mice. Same results for matn-1.



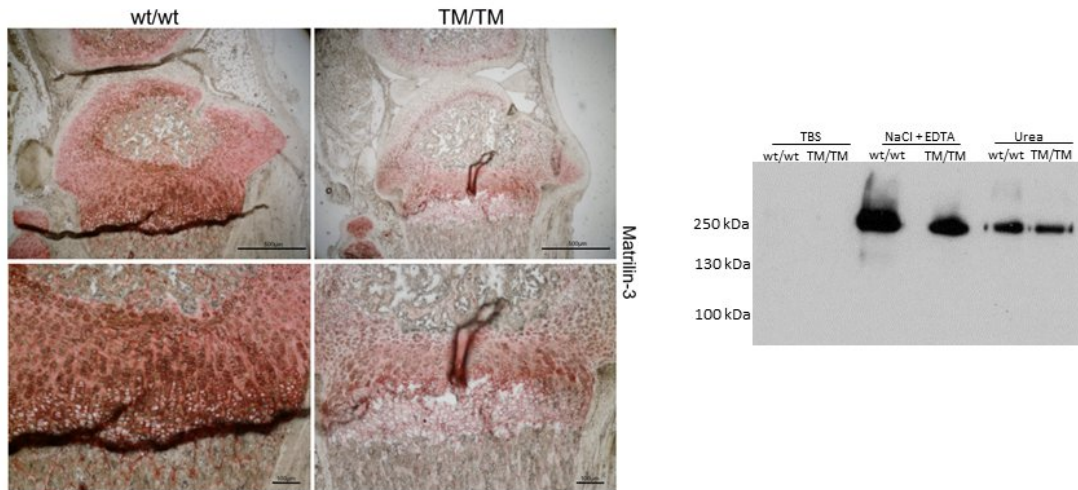
2 weeks.tif

Knees of wt and matn3 T298M mutant were stained via IHC (Fast Red). 2-weeks old animals. Protein extraction from 2-weeks old knees. Decreased Matn-3

SYBIL Project 602300. The SYBIL Project is funded under the European Commission Seventh Framework Programme, grant number 602300, Theme HEALTH.2013.2.1.1-1



signal in 2-weeks old mutant mice. Decreased Matn-3 protein level in mutant mice. Same results for matn-1.

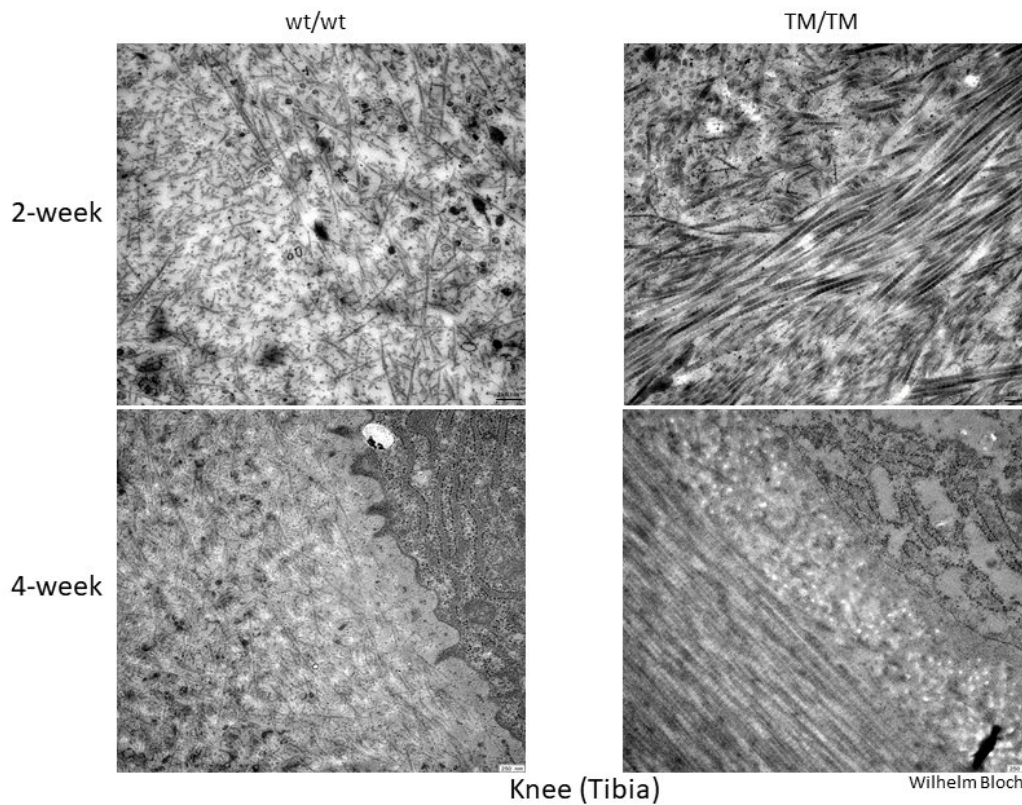


2 weeks knee.tif

EM analysis of the knee (Tibia) of 2- and 4-weeks old animals. Increased fibril diameter were detected in

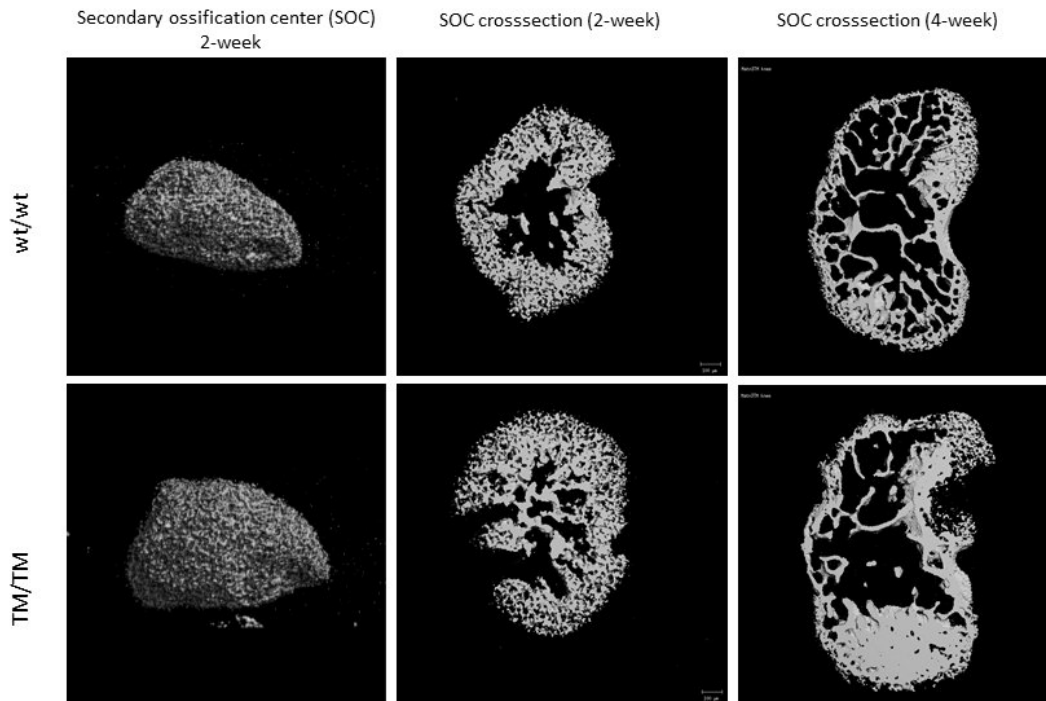


mutant mice. It seems to be that the mutation has an impact on collagen fibrillogenesis.



EM 2 and 4 weeks old knees.tif

MicroCT analysis of 2- and 4-weeks old knees. Secondary ossification center (SOC) of the mutant mice is increased in width. SOC crosssection revealed an impact on the ossification in 2- and 4-weeks old mutant mice.



Juliane Heilig, Anja Niehoff

microCT 2 and 4 weeks old knees.tif

**Transcriptome analyses of 1-week old animals
revealed a link to the TGF- β /BMP-2 pathway.**

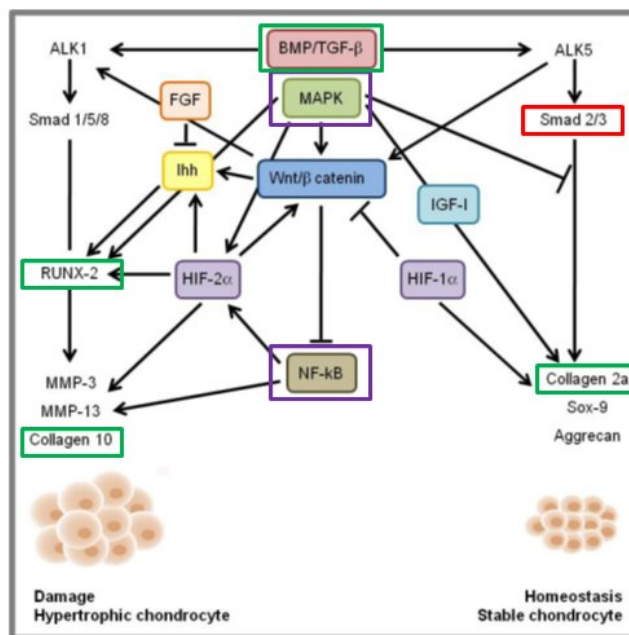


Upregulation of BMP-2, RUNX-2 and Collagen-10 in mutant mice.

Transcriptome Analysis (1-week-old animals)

1-week			
Gene	WT	Mut	
Matn1	111.424	0.993578	▼
Matn3	124.111	107.801	▼
Sox9	210.147	235.829	
Col2a1	39.597	472.941	▲
Col10a1	52.337	468.352	▲
Bmp2	34.777	344.926	▲
Tgfb1	362.211	427.722	▲
Smad1	171.954	154.866	
Smad2	743.571	767.455	
Smad3	282.419	11.312	▼
Smad3	171.115	134.316	▼
Smad3	17.047	0.963375	▼
Smad5	160.066	159.968	
Runx2	0.660103	113.296	▲
MMP13	220.932	227.298	

Knee (Tibia)



(Mariani et al., 2014)

Transcriptome analysis 1 week.tif

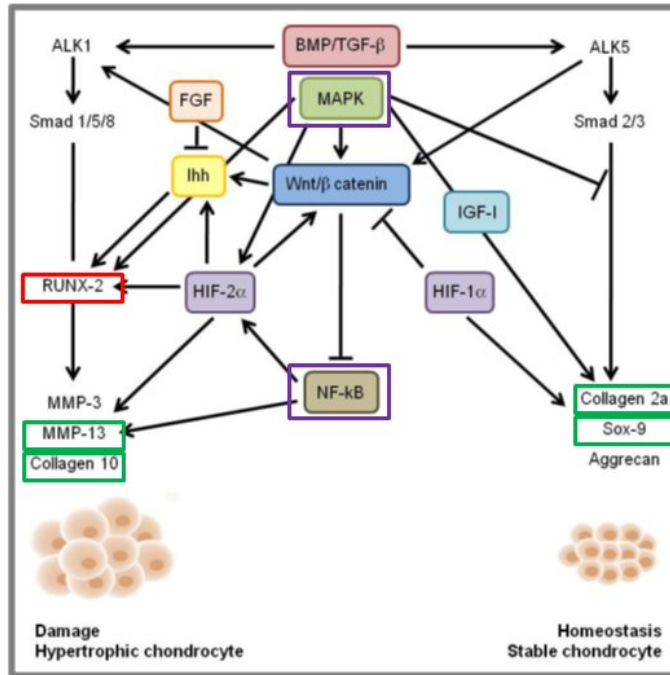
Transcriptome analyses of 2-week old animals revealed a link to the TGF-β/BMP-2 pathway. Upregulation of Sox-9 in mutant mice.



Transcriptome Analysis (2-week-old animals)

2-week			
Gene	WT	Mut	
Matn1	252.136	349.165	^
Matn3	146.119	23.139	v
Sox9	44.273	353.691	^
Col2a1	155.863	525.337	^
Col10a1	103.662	159.371	^
Bmp2	511.165	537.174	
Tgfb1	756.243	727.698	
Smad1	165.098	151.361	
Smad2	518.907	509.883	
Smad3	223.736	134.894	v
Smad3	179.102	194.733	
Smad3	240.663	270.375	
Smad5	177.073	181.301	
Runx2	446.511	367.275	v
MMP13	238.683	302.178	^

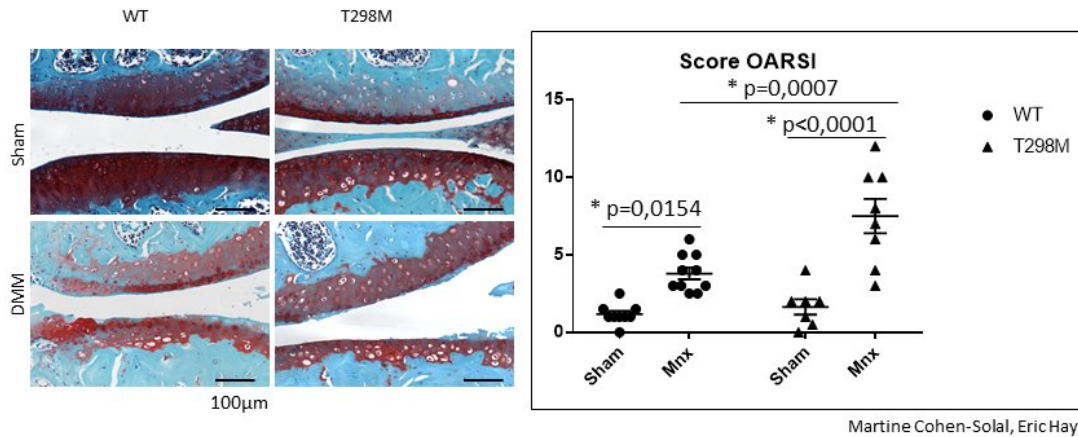
Knee (Tibia)



(Mariani et al., 2014)

Transcriptome analysis 2 week.tif

Premature osteoarthritis in mutant mice by DMM. WT Oarsie score 3.8 and mutant Oarsie score 7.4.



Martine Cohen-Solal, Eric Hay

WT score: 3.8
T298M score: 7.4

DMM OA Mutant.tif