



Search for novel senolytic drugs for rescue of osteoarthritis

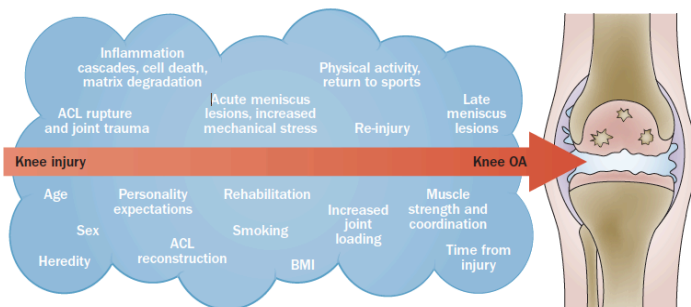
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Challenge: Sharp growth of aged population calls for a rethink how our healthcare should be delivered for age-related pathologies, including osteoarthritis, a leading cause of pain and disability in older adults.

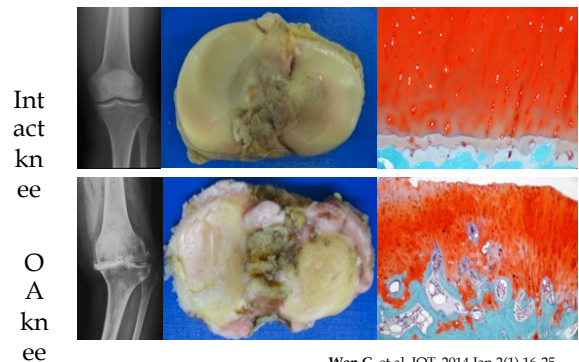
Mission: Early diagnosis and intervention of OA to promote active ageing

The etiology of knee OA is multifactorial



Wen C, Lohmander LS. Nat Rev Rheumatol. 2014 Oct;10(10):577-8.

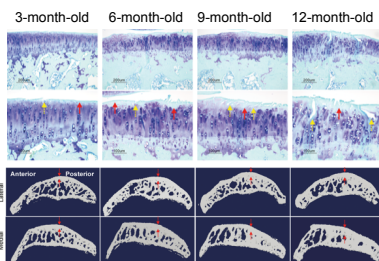
“Osteo” arthritis: A Bone Problem?



Wen C et al. JOT, 2014 Jan 2(1) 16-25.

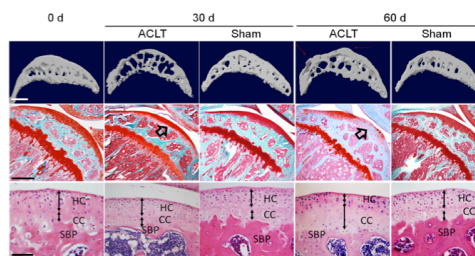
Research & Development Platform:

Spontaneous OA model



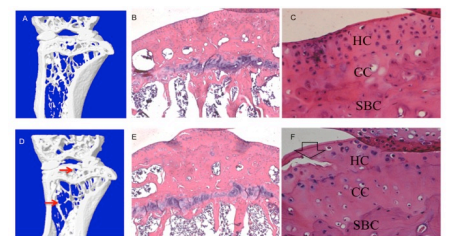
Wang T, et al., Osteoarthritis Cartilage. 2013 Apr;21(4):574-81.
Zhao W et al., J Orthop Res. 2015 Oct 23.

Surgery-induced OA model



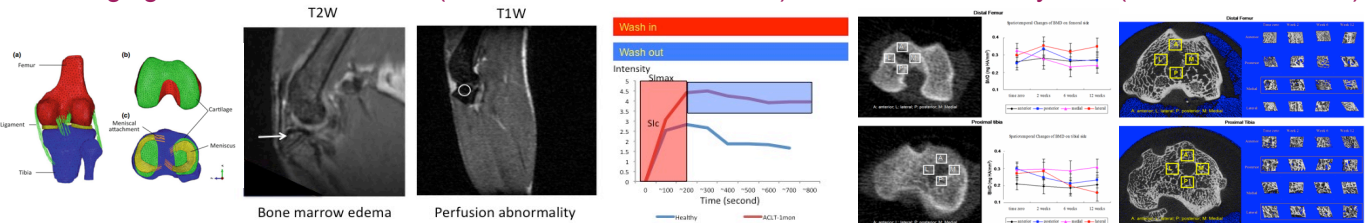
Zhen G, Wen C, et al. Nat Med. 2014 Oct;10(10):577-8.

Transgenic OA model



Wen C, et al. Life Sci. 2014

Multi-imaging modalities: VivaCT40 (Scanco, CAF, 14/F Y Block); Vevo LAZR 2100 system (VisualSonic, Y505)



Yao J, Wen C, et al., Ann Biomed Eng. 2012 Jul;40(7):1554-67.

Zhen G, Wen C, et al. Nat Med. 2014 Oct;10(10):577-8.

Wen C et al., J Orthop Res. 2010 Jan; 28(1): 70-6.

Patent:

- Chondroitin sulfate Strontium and its preparation method (CN 104788586 A)

Patent:

PI for Health and Medical Research Fund - Research Fellowship Scheme “Photoacoustic Molecular Imaging of Osteoarthritic Pain – a Proof-of-concept Study” (#01150087)

Co-I for RGC General Research Fund Scheme - “Is endothelin-1 signaling a therapeutic target to rescue OA? An experimental study” (#7105314)

Publications

Osteoarthritis

- (1) Huang YP, Zhong J, Chen J, Yan CH, Zheng YP, Wen CY. High frequency ultrasound imaging of tidemark in vitro in advanced knee osteoarthritis. **Ultrasound in Medicine and Biology** (accepted)
- (2) Chan B, Wen CY. Spontaneous hypertensive rat exhibits bone and meniscus phenotypes of osteoarthritis: is it an appropriate control for MetS-associated OA? **Annals of the Rheumatic Diseases** 2017 Aug 10. pii: annrheumdis-2017-211995. doi: 10.1136/annrheumdis-2017-211995.
- (3) Ma, F, Liu N, Hu N, Wen CY, Tang B. "Synthesis of strontium chondroitin sulfate and the evaluation of its capability to attenuate osteoarthritis". **Carbohydrate Polymers**, 2017(170): 217-225.
- (4) Zhao W, Wang T, Luo Q, Chen Y, Leung VY, **Wen C**, Shah MF, Pan H, Chiu K, Cao X, Lu WW. Cartilage degeneration and excessive subchondral bone formation in spontaneous osteoarthritis involves altered TGF- β signaling. **J Orthop Res**. 2016 May;34(5):763-70.
- (5) Sin A, Tang W, **Wen C**, Chung SK, Chiu KY. The emerging role of endothelin-1 in the pathogenesis of subchondral bone disturbance and osteoarthritis. **Osteoarthritis & Cartilage** 2015 Apr;23(4):516-24.
- (6) **Wen, C.** & Lohmander, L. S. Does post-injury ACL reconstruction prevent future OA? **Nat. Rev. Rheumatol**. 2014 Oct;10(10):577-8.
- (7) Chan P, Zhu L, **Wen CY**, Chiu KY. Subchondral bone proteomics in osteoarthritis: Current status and perspectives. **Journal of Orthopaedic Translation** 2015: 3 (2), 71-77
- (8) Tang B, Fong MK, **Wen CY**, Yan CH, Chan D, Ngan A, Chiu KY, Lu WW. Nanostiffness of Collagen Fibrils Extracted From Osteoarthritic Cartilage Characterized with AFM Nanoindentation. **Soft Materials** 2014 12(3) 253-261.
- (9) **Wen CY**, Lu W, Chiu KY. Importance of subchondral bone in pathogenesis and management of osteoarthritis - from bed to bench. **Journal of Orthopaedic Translation** 2014 Jan 2(1) 16-25.
- (10) **Wen C**, Chen Y, Tang HL, Yan CH, Lu WW, Chiu KY. Bone loss at subchondral plate in knee osteoarthritis patients with hypertension and type 2 diabetes mellitus. **Osteoarthritis & Cartilage**. 2013 Nov; 21(11): 1716-23.
- (11) Zhen GH, **Wen CY**, Jia XF, Li Y, Mears S, Askin F, Frassica F, Chang W, Crane J, Yao J, Nayfeh T, Johnson C, Artemov D, Cosgarea A, Carrino J, Wan M, Lu W and Cao X. Inhibition of TGF β signaling in subchondral bone mesenchymal stem cells prevents onset of osteoarthritis. **Nature Medicine** 2013 Jun; 19(6): 704-12.
- (12) Wang T, **Wen CY**, Yan CH, Lu WW, Chiu KY. Spatial and Temporal Changes of Subchondral Bone Proceeds to Articular Cartilage Degeneration in Guinea Pigs with Spontaneous Osteoarthritis. **Osteoarthritis & Cartilage** 2013 Apr; 21(4): 574-81.
- (13) **Wen CY**, Wu CB, Tang B, Wang T, Yan CH, Lu WW, Pan H, Hu Y, Chiu KY. Collagen Fibril Stiffening in Osteoarthritic Cartilage of Human Beings Revealed by Atomic Force Microscopy. **Osteoarthritis & Cartilage**. 2012 Aug; 20(8): 916-22.

Osteoporosis

- (14) Liu ZY, Yang, Y, Wen CY, Rong LM "Serum Osteocalcin and Testosterone Concentrations in Adult Males with or without Primary Osteoporosis: A Meta-Analysis". **BioMed Research International**, 2017 (in print)
- (15) Qiu T, Xian L, Crane J, **Wen C**, Hilton M, Newman P, Lu W, Cao X. PTH receptor signaling in osteoblasts regulates endochondral vascularization in maintenance of postnatal growth plate. **J Bone Miner Res**. 2015 Feb; 30 (2):309-17.
- (16) Xian LL, Lou M, Wu XW, Yu B, Frank Frassica F, Wan M, Pang LJ, **Wen CY**, Tryggestad E, Wong J, Xu Cao X. Pretreatment with antioxidants prevent bone injury by improving bone marrow microenvironment for stem cells. **Stem Cell Discovery** 2012 July 2(3): 100-107.
- (17) Cao X, Wu X, Frassica D, Yu B, Pang L, Xian L, Wan M, Lei W, Armour M, Tryggestad E, Wong J, **Wen CY**, Lu WW, Frassica FJ. Irradiation induces bone injury by damaging bone marrow microenvironment for stem cells. **Proc Natl Acad Sci U S A**. 2011 Jan 25; 108(4): 1609-14.
- (18) Shen YH, Liu WC, **Wen CY**, Pan HB, Wang T, Darvell BW, Lu WW, Huang WH. Local pH in Bone Regeneration: Strontium-doped Borosilicate Scaffold. **Journal of Materials Chemistry** 2012 (22) 8662-8670.

- (19) Shen Y, Liu W, Lin K, Pan H, Darvell BW, Peng S, **Wen C**, Deng L, Lu WW, Chang J. Interfacial pH – a critical factor for osteoporotic bone regeneration. *Langmuir*, 2011, 27 (6), pp 2701–2708.

Tendon & Ligament Injury

- (20) Yao J, **Wen CY**, Zhang M, Cheung JT, Yan C, Chiu KY, Lu WW, Fan Y. Effect of tibial drill-guide angle on the mechanical environment at bone tunnel aperture after anatomic single-bundle anterior cruciate ligament reconstruction. *International Orthopaedics*. 2014 May; 38(5): 973-81.
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- (22) Peng J, **Wen C***, Wang A, Wang Y, Xu W, Zhao B, Zhang L, Lu S, Qin L, Guo Q, Dong L, Tian J. Micro-CT based Bone Ceramic Scaffolding and its Performance when Seeded by Marrow-Derived Mesenchymal Stem Cells for Reconstruction of Load-bearing Bone of Femoral Head in A Canine Model. *J Biomed Mater Res B Appl Biomater*. 2011 Feb; 96(2): 316-25.
- (23) **Wen CY**, Qin L, Lee KM, Wong MW, Chan KM. Grafted tendon healing in tibial tunnel is inferior to healing in femoral tunnel after anterior cruciate ligament Reconstruction: a histomorphometric study in rabbits. *Arthroscopy*. 2010 Jan; 26(1): 58-66.
- (24) Qin L, Wang L, Wong MW, **Wen C**, Wang G, Zhang G, Chan KM, Cheung WH, Leung KS. Osteogenesis induced by extracorporeal shockwave in treatment of delayed osteotendinous junction healing. *J Orthop Res*. 2010 Jan; 28(1): 70-6.
- (25) **Wen CY**, Qin L, Lee KM, Wong MW, Chan KM. Influence of bone adaptation on tendon-to-bone healing in bone tunnel after anterior cruciate ligament Reconstruction in a rabbit model. *J Orthop Res*. 2009 Nov; 27(11): 1447-56.
- (26) **Wen CY**, Qin L, Lee KM, Chan KM. The use of brushite calcium phosphate cement for enhancement of bone-tendon integration in an anterior cruciate ligament reconstruction rabbit model. *J Biomed Mater Res B Appl Biomater*. 2009 May; 89B(2): 466-74.
- (27) **Wen CY**, Qin L, Lee KM, Chan KM. Peri-graft bone mass and connectivity as Predictors for the strength of tendon-to-bone attachment after anterior cruciate Ligament reconstruction. *Bone*. 2009 Sep; 45(3): 545-52.

Spinal Cord injury

- (28) **Wen CY**, Cui JL, Mak KC, Luk DK, Hu Y. Diffusion Tensor Imaging of Somatosensory Tract in Cervical Spondylotic Myelopathy and Its Link with Electrophysiological Evaluation. *Spine J* 2014 Aug 1;14(8):1493-500.
- (29) **Wen CY**, Liu HS, Cui JL, Mak KC, Cheung WY, Hu Y, Luk DK. Is Diffusion Anisotropy A Biomarker for Disease Severity and Surgical Prognosis of Cervical Spondylotic Myelopathy? *Radiology* 2014 Jan; 270(1):197-204.
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- (31) Long HQ, Li GS, Hu Y, **Wen CY**, Xie WH. HIF-1 α /VEGF signaling pathway may play a dual role in secondary pathogenesis of cervical myelopathy. *Med Hypotheses*. 2012 Jul; 79(1): 82-4.
- (32) Cui JL, **Wen CY**, Hu Y, Mak KC, Mak KH, Luk KD. Orientation entropy analysis of diffusion tensor in healthy and myelopathic spinal cord. *Neuroimage*. 2011 Oct 15; 58(4): 1028-33.
- (33) Hu Y, **Wen CY**, Li TH, Cheung MM, Wu EX, Luk KD. Somatosensory-Evoked Potentials as an Indicator for the Extent of Ultrastructural Damage of Spinal Cord after Chronic Compressive Injuries in a Rat Model. *Clin Neurophysio*. 2011 Jul; 122(7): 1440-7.
- (34) Cui JL, **Wen CY**, Hu Y, Li TH, Luk KD. Entropy-based Analysis for Diffusion Anisotropy Mapping of Healthy and Myelopathic Spinal Cord. *Neuroimage*. 2011 Feb 1; 54(3): 2125-31.