

## Supplementary Material

### Translational evaluation of gait behavior in rodent models of arthritic disorders with the CatWalk device - a narrative review

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#### 1 Supplementary Tables

**Supplementary Table S1.** Studies evaluating Osteoarthritis by means of the CW system (n=32).

Biochemically induced Osteoarthritis (n=19)

| Reference      | Rodent | Joint (Side) | Induction method | Treatment                       | Strain   | Sex | Follow up | Additional Analysis besides CW                                                                                                                                | Assessed CW parameters    |
|----------------|--------|--------------|------------------|---------------------------------|----------|-----|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| Adaes 2014 (1) | rat    | Knee (LH)    | Collagenase      | Morphine, Lidocaine, Diclofenac | W (n=99) | ♂   | 6w        | Knee-Bend Test, Knee diameter, Histopathology, Immunofluorescence for TRPV1                                                                                   | Total Paw Print Intensity |
| Adaes 2015 (2) | rat    | Knee (LH)    | Collagenase      | Gabapentin                      | W (n=73) | ♂   | 6w        | Knee-Bend Test, Knee diameter, Histopathology, Immunofluorescence for ATF-3, NPY and SP, Expression of voltage-gated calcium channel subunit $\alpha 2\delta$ | Total Paw Print Intensity |

|                          |      |           |                    |                                 |                                         |   |     |                                                                                                                                 |                                                                           |
|--------------------------|------|-----------|--------------------|---------------------------------|-----------------------------------------|---|-----|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Ko 2016 (3)              | mice | Knee (LH) | Collagenase        | HSP60                           | TgHSP60 (n=27), WT (n=27), FVB/N (n=48) | ♂ | 8w  | RT-PCR analysis, Immunoblotting, Histomorphometry Immunohistochemistry, $\mu$ CT, Near-infrared in vivo fluorescence imaging    | Max Contact Area, Max Intensity at Max Contact, Max Intensity, Print Area |
| Adaes 2017 (4)           | rat  | Knee (LH) | Collagenase        | Fluorocitrate                   | W (n=37)                                | ♂ | 6w  | Knee-Bend Test, Immunohistochemical analysis of GFAP, ATF3 IBA-1, Western Blot                                                  | Total Paw Print Intensity                                                 |
| Ferreira-Gomes 2008 (5)  | rat  | Knee (LH) | MIA                |                                 | W (n=?)                                 | ♂ | 31d | Knee-Bend Test, Pin-Prick Test, Von Frey Test, Randall-Selitto Test, Histology                                                  | Total Paw Print Intensity                                                 |
| Ferland 2011 (6)         | rat  | Knee (LH) | ACLT + pMMx or MIA | Celecoxib                       | SD (n=40)                               | ♂ | 4w  | Von Frey Test, Histology, Neuropeptide analysis of SP and CGRP                                                                  | Swing Time, Swing Speed, Duty Cycle                                       |
| Ferland 2012 (7)         | rat  | Knee (LH) | MIA                | Eugenol                         | SD (n=23)                               | ♂ | 4w  | Von Frey Test, Neuropeptide analysis of SP, CGRP, Dynorphin, Histology, Toxicological assessment, Histopathology, Knee diameter | Swing Time, Swing Speed, Duty Cycle                                       |
| Ferreira-Gomes 2012a (8) | rat  | Knee (LH) | MIA                | Lidocaine, Morphine, Diclofenac | W (n=?)                                 | ♂ | 20d | Histology, Knee-Bend Test                                                                                                       | Total Paw Print Intensity                                                 |
| Ferreira-Gomes 2012b (9) | rat  | Knee (LH) | MIA                |                                 | W (n=?)                                 | ♂ | 31d | Knee Bend Test, Histology, Immunohistochemistry for ATF-3, NPY, GAP-43                                                          | Total Paw Print Intensity                                                 |

|                       |      |              |     |                                                            |                                 |   |      |                                                                                                                                                                                              |                                                                               |
|-----------------------|------|--------------|-----|------------------------------------------------------------|---------------------------------|---|------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| Ishikawa<br>2014 (10) | rat  | Knee<br>(RH) | MIA | Diclofenac,<br>Morphine,<br>Tramadol,<br>Duloxetine        | SD (n=?)                        | ♂ | 3w   | Incapacitance Test                                                                                                                                                                           | Max Contact<br>Area, Swing<br>Speed                                           |
| Ishikawa<br>2015 (11) | rat  | Knee<br>(RH) | MIA | Anti-NGF<br>antibody                                       | SD (n=?)                        | ♂ | 35d  | ELISA based binding activities<br>evaluation assay, Cell-based<br>NGF function evaluation assay,<br>Plasma concentration of Anti-<br>NGF antibody; Knee diameter,<br>Scoring of knee lesions | Max Contact<br>Area, Swing<br>Speed                                           |
| Miyagi<br>2017 (12)   | mice | Knee<br>(RH) | MIA | Anti-NGF<br>antibody                                       | C57BL/6<br>(n=30)               | ♂ | 5w   | Immunohistochemistry for<br>CGRP                                                                                                                                                             | Duty Cycle,<br>Swing Speed,<br>Print Area                                     |
| Miyamoto<br>2017 (13) | rat  | Hip<br>(RH)  | MIA |                                                            | SD<br>(n=60)                    | ♂ | 56d  | Immunohistochemistry for<br>CGRP and ATF3                                                                                                                                                    | 21 CW<br>parameters*                                                          |
| Carcole<br>2019 (14)  | mice | Knee<br>(?)  | MIA | Sigma-1<br>receptor<br>antagonist                          | Swiss-<br>albino CD<br>1 (n=53) | ♂ | 25d  | Von Frey Test, NORT,<br>Elevated plus maze, Elevated<br>zero-maze test, Forced<br>swimming test, Histology,<br>Immunofluorescence                                                            | Print Area, Max<br>Contact Area,<br>Swing Time,<br>Duty Cycle                 |
| Tschon<br>2020 (15)   | rat  | Knee<br>(RH) | MIA | Hyaluronic<br>acid-chitlac,<br>Triamcinolone<br>acetoneide | SD<br>(n=80)                    | ♂ | 21d  | PAM, Histology,<br>Immunohistochemistry for type<br>II collagen and aggrecan                                                                                                                 | Print Area, Stand<br>Time, Swing<br>Time, Single<br>Stance                    |
| Caglar<br>2021 (16)   | rat  | Knee<br>(LH) | MIA | Astaxanthin,<br>Corticosteroid,<br>Hyaluronic acid         | W (n=44)                        | ♂ | 8w ? | Histology                                                                                                                                                                                    | Print Length,<br>Print Width,<br>Print Area,<br>Stride Length,<br>Stand Time, |

|                          |     |           |     |                           |            |   |     |                                                                                |                                                                                                                                                              |
|--------------------------|-----|-----------|-----|---------------------------|------------|---|-----|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                          |     |           |     |                           |            |   |     |                                                                                | Max Contact Intensity, Run Duration, Average Speed, Swing Speed                                                                                              |
| Ferreira-Gomes 2021 (17) | rat | Knee (LH) | MIA | Synthetic TLR4 Antagonist | W (n=20)   | ♂ | 28d | Knee-Bend Test, Immunohistochemical analysis for TLR4 and ATF3, Histopathology | Total Paw Print Intensity                                                                                                                                    |
| Kara 2021 (18)           | rat | Knee (LH) | MIA |                           | W (n=10)   | ♂ | 4w  | Manual walking platform for gait analysis, Histology                           | Print Length, Print Width, Stride Length, Average Speed, Run Duration, Maximum Contact Intensity, Print Area, Stand Time, Swing Speed                        |
| Han 2022 (19)            | rat | Knee (LH) | MIA |                           | SD (n=54?) | ♂ | 42d | Von Frey Test, Pressure algometry                                              | Stand Time, Print Area, Swing Speed, Duty Cycle, Single Stance, Phase Dispersion, Dynamic Weight bearing, Dynamic Weight Bearing (%), Dynamic Guarding Index |

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|--|--|--|--|--|--|--|--|--|-----|
|  |  |  |  |  |  |  |  |  | (%) |
|--|--|--|--|--|--|--|--|--|-----|

### Surgically induced Osteoarthritis (n=12)

| Reference          | Rodent | Joint (Side) | Induction method                    | Treatment                            | Strain                  | Sex | Follow up | Additional Analysis besides CW                                                                                                                                         | Assessed CW parameters                                                  |
|--------------------|--------|--------------|-------------------------------------|--------------------------------------|-------------------------|-----|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Fu 2012 (20)       | rat    | Knee (RH)    | ACLT                                | Buprenorphine                        | SD (n=18)               | ♀   | 6m        | μCT, Histology                                                                                                                                                         | Limb Idleness Index, Target Print Ratio, Anchor Print Ratio, Swing Time |
| Cheuk 2016 (21)    | rat    | Knee (RH)    | ACLT                                | Vitamin C + Quercetin + Deferoxamine | SD (n=12)               | ♀   | 25w       | μCT, Histology                                                                                                                                                         | Limb Idleness Index                                                     |
| Siu 2019 (22)      | rat    | Knee (RH)    | ACLT + resection of medial meniscus | DAEP (Chinese herbal paste)          | SD (n=28)               | ♂   | 8w        | Incapacitance Test, X-ray, Western Blot, qPCR (IL-6, TNF-α, iNOS, COX-2 and MMP-3), Quantitative analysis of the chemical markers of the DAEP and transdermal property | Stand Time, Print Area, Max Intensity, Swing Speed, Duty Cycle          |
| Zhu 2020 (23)      | mice   | Knee (LH)    | ACLT                                |                                      | C57/B6 (n=?)            | ♂   | 6m        | Histology, μCT, Von Frey Test, Western Blot                                                                                                                            | Stand Time, Max Intensity at Max Intensity                              |
| Brenneis 2020 (24) | rat    | Knee (RH)    | ACLT + resection of medial          |                                      | Lister Hooded (Crl:LIS) | ♂   | 20w       | ELISA (AGNx1 in serum), Joint diameter,                                                                                                                                | Relative Print Length (%)                                               |

|                                     |      |                                       |                                                                                                |                            |                                                     |         |     |                                                                                                           |                                                                                                                                                |
|-------------------------------------|------|---------------------------------------|------------------------------------------------------------------------------------------------|----------------------------|-----------------------------------------------------|---------|-----|-----------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
|                                     |      |                                       | meniscus or<br>MMT or<br>DMM                                                                   |                            | outbred SPF<br>(n=?)                                |         |     | Quantification of joint<br>flexibility,<br>Spontaneous activity,<br>Histopathology, $\mu$ CT              |                                                                                                                                                |
| Malfait 2010<br>(25)                | mice | Knee<br>(RH)                          | DMM                                                                                            | Morphine,<br>Acetaminophen | CD-1,<br>C57BL/6,<br>ADAMTS-<br>5 knockout<br>(n=?) | ♂,<br>♀ | 56d | Von Frey Test,<br>Histology, Radiant<br>heat paw withdrawal<br>test, Overnight<br>locomotor activity test | Mean Intensity at<br>Max Contact                                                                                                               |
| Muramatsu<br>2014 (26)              | mice | Knee<br>(LH)                          | DMM                                                                                            | Hyaluronan                 | C57BL/6<br>(n=60)                                   | ♂       | 16w | Histology                                                                                                 | 21 CW parameters*                                                                                                                              |
| Fang 2018<br>(27)                   | mice | Knee<br>(LH)                          | DMM                                                                                            |                            | C57/BL6<br>(n=?)                                    | ?       | 10w | $\mu$ CT, Histology                                                                                       | Paw Intensity                                                                                                                                  |
| Fouasson-<br>Chailloux<br>2021 (28) | mice | Knee<br>(RH)<br>or Bilateral<br>knees | DMM<br>(Unilateral and<br>bilateral)                                                           |                            | C57BL/6<br>(n=24)                                   | ♂       | 16w | $\mu$ CT, Histology                                                                                       | Average Speed,<br>Print Area, Paw<br>Print Intensity,<br>Stand Time, Swing<br>Time, Swing Speed,<br>Duty Cycle                                 |
| Westhof<br>2021 (29)                | rat  | Knee<br>(RH)                          | DMM                                                                                            | Zilretta                   | SD (n=95)                                           | ♀       | 91d | Jump Incapacitance,<br>Joint diameter                                                                     | Relative Print<br>Length (%)                                                                                                                   |
| Zahoor 2016<br>(30)                 | rat  | Knee<br>(LH)                          | Intraarticular<br>fracture of the<br>medial tibial<br>plateau +<br>internal<br>fixation with 2 |                            | SD (n=8)                                            | ♂       | 8w  | Histology                                                                                                 | Initial Contact<br>Time, Maximal<br>Contact Time, Max<br>Print Area, Print<br>Area, Stride Length,<br>Print Width, Print<br>Length, Intensity, |

|                  |     |           |                                                                                         |                                 |           |   |    |           |                                                                                                                                                                                                         |
|------------------|-----|-----------|-----------------------------------------------------------------------------------------|---------------------------------|-----------|---|----|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                  |     |           | needles                                                                                 |                                 |           |   |    |           | Stand Time, Swing Time, Duty Cycle, Swing Speed, Paw Angle, Stand Index                                                                                                                                 |
| Zahoor 2017 (31) | rat | Knee (LH) | Intraarticular fracture of the medial tibial plateau + internal fixation with 2 needles | Low-Intensity pulsed ultrasound | SD (n=30) | ♂ | 8w | Histology | Initial Contact Time, Maximal Contact Time, Stride Length, Max Print Area, Print Width, Print Length, Stand Time, Swing Time, Duty Cycle, Intensity Paw Angle Movement Vector, Swing Speed, Stand Index |

LH: Left hindlimb, RH: Right hindlimb, W: Wistar, SD: Sprague Dawley, w: weeks, d: days, h: hours, m: months, TgHSP60: Heat shock protein 60 transgenic mice, WT: Wild-type, HSP60: Heat shock protein 60, TRPV1: transient receptor potential vanilloid 1, ATF-3: activating transcription factor-3, NPY: Neuropeptide Y, SP: Neuropeptide Substance P (SP), GFAP: Glial fibrillary acidic protein, IBA-1: ionized calcium-binding adapter molecule 1, MIA: Monoiodoacetate, ACLT: Anterior cruciate ligament transection, pMMx: Partial medial meniscectomy, CGRP: Calcitonin gene related peptide, GAP-43: Growth associated protein GAP-43, NGF: Nerve growth factor, NORT: Novel object recognition task, PAM: Pressure Application Measurement, TLR4: Toll-like receptor 4, IL6: Interleukin-6, TNF- $\alpha$ : Tumor necrosis factor  $\alpha$ , iNOS: Inducible nitric oxide synthase, COX-2: Cyclooxygenase-2, MMP-3: Matrix metalloproteinase-3, MMT: Medial meniscal tear, DMM: Destabilization of medial meniscus, AGNx1: Marker of cartilage extracellular matrix remodeling, ADAMTS: A Disintegrin and Metalloproteinase with Thrombospondin Motif

\*The analyzed parameters are not further specified, only significantly altered parameters are listed.

**Supplementary Table S2.** Studies investigating Monoarthritis via the CW system (n=9).

| Reference                | Rodent | Joint (Side)           | Induction method | Treatment           | Strain                                      | Sex | Follow up | Additional Analysis besides CW                                                     | Assessed CW parameters                                                                                                                                                                                                    |
|--------------------------|--------|------------------------|------------------|---------------------|---------------------------------------------|-----|-----------|------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Gabriel 2007 (32)        | rat    | Knee (RH)              | CARR             |                     | SD (n=30)                                   | ♂   | 48h       | Von Frey Test                                                                      | Mean Intensity, Duty Cycle, Base of Support, Relative Paw Placements, Max Contact Area, Print Area, Print Width, Print Length, Swing Speed, Step Cycle, Stride Length, Regularity Index, Phase Lag, Phase Lag Variability |
| Angeby-Moeller 2008 (33) | rat    | Tibiotarsal joint (LH) | CARR             | Morphine, Rofecoxib | SD (n=48)                                   | ♂   | 24h       | None                                                                               | Print Area, Mean Intensity, Duty Cycle, Regularity Index                                                                                                                                                                  |
| Gabriel 2009 (34)        | rat    | Knee (RH)              | CARR             |                     | SD (n=24)                                   | ♂   | 4w        | Von Frey Test                                                                      | Mean Intensity, Duty Cycle                                                                                                                                                                                                |
| Pinho 2011 (35)          | rat    | Tibiotarsal joint (LH) | CFA              |                     | W (n=16), SD (n=26), SHR (n=13), WKY (n=13) | ♂   | 16d       | Von Frey Test, Ankle-Bend Test, Fos expression, Inflammation score, Ankle diameter | Arthritic Paw Load (%)                                                                                                                                                                                                    |
| Parvathy 2013 (36)       | mice   | Ankle (RH)             | CFA              | Indomethacin        | C57BL/6 (n=55)                              | ♀   | 7d        | None                                                                               | Regularity Index, Mean Intensity at Max Contact, Print                                                                                                                                                                    |



|                          |      |                               |                   |                                                                                |                                |   |     |                                                                 |                                                                                                                                 |
|--------------------------|------|-------------------------------|-------------------|--------------------------------------------------------------------------------|--------------------------------|---|-----|-----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|
|                          |      |                               |                   |                                                                                |                                |   |     |                                                                 | Area, Stand Time, Stride Length, Swing Time, Duty Cycle, Swing Speed                                                            |
| Angeby Moeller 2018 (37) | rat  | Tibiotarsal joint (LH)        | CFA               | Naproxen, Pregabalin                                                           | W (n=104)                      | ♂ | 4d  | Incapacitance Test, Von Frey Test                               | Regularity Index, Walking Speed, Duty Cycle, Dynamic Weight Bearing, Dynamic Weight Bearing (%), Dynamic Guarding Index (%)     |
| Angeby Moeller 2020 (38) | mice | OA: Knee (LH); MA: Ankle (LH) | OA: ACLT, MA: CFA | Anti-NGF antibody                                                              | C57BL/6JRj (n=181)             | ♀ | 14d | Histopathology, Stationary weight bearing, Ankle joint swelling | Regularity Index, Walking Speed, Duty Cycle, Swing Speed, Stride Length, Weight bearing, Weight bearing (%), Guarding index (%) |
| Masocha 2009 (39)        | mice | Ankle (RH)                    | LPS               | Indomethacin                                                                   | C57BL/6 (n=71)                 | ? | 7d  | None                                                            | Mean Intensity at Max Contact, Print Area, Regularity Index                                                                     |
| Abu-Ghefreh 2010 (40)    | mice | Ankle (RH)                    | LPS               | Minocycline, Indomethacin, Selective COX1 inhibitor, Selective COX 2 Inhibitor | BALB/c (n=338), C57BL/6 (n=32) | ? | 2d  | Hot Plate Test                                                  | Mean Intensity at Max Contact, Print Area                                                                                       |

CARR: Carrageenan, CFA: Complete Freund's adjuvant, LPS: Lipopolysaccharide, LH: Left hindlimb, RH: Right hindlimb, W: Wistar, SD: Sprague Dawley, w: weeks, d: days, h: hours, SHR: Spontaneously hypertensive rats, WKY: normotensive Wistar Kyoto rat, OA: Osteoarthritis, MA: Monoarthritis, NGF: Nerve growth factor, ACLT: Anterior cruciate ligament transection

**Supplementary Table S3.** Studies investigating polyarthritic disorders via the CW system (n=3).

| Reference                   | Rodent | Type of injury       | Induction method | Treatment                      | Strain             | Sex   | Follow up                                           | Additional Analysis besides CW                                                                                                                                | Assessed CW parameters                                                                                                                                                  |
|-----------------------------|--------|----------------------|------------------|--------------------------------|--------------------|-------|-----------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Hayer 2016 (41)             | mice   | Rheumatoid Arthritis | hTNFtg mice      | Anti-TNF antibody (Infliximab) | hTNFtg, WT (n=?)   | ♀     | Week 5 after birth until end of week 15 after birth | Paw Swelling, Grip strength, $\mu$ -CT, Histopathology                                                                                                        | Print Area, Print Length, Print Width, Max Contact Area, Stride Length, Swing Speed, Max Intensity, Mean Intensity, Regularity Index, Phase Dispersion, Print Positions |
| Mausset-Bonnefont 2019 (42) | mice   | Rheumatoid Arthritis | Collagen type II | Methotrexate                   | DBA/1OlaHsd (n=91) | ♂     | 49d                                                 | Open Field Test, Von Frey Test, Hargreaves Test, Static weight-bearing, Skin Temperature, $\mu$ -CT, Histopathology, Paw swelling, Clinical Arthritis Scoring | Print Area, Max Intensity, Stand Time, Stride Length, Run Duration                                                                                                      |
| Hoffman 2010 (43)           | rat    | Polyarthritis        | Pristane         |                                | DA (n=?)           | ♂ / ♀ | 35d                                                 | Histology, Histomorphometry                                                                                                                                   | Print Area, Stand Time, Regularity Index                                                                                                                                |

WT: Wild-type, d: days, TNF: Tumor necrosis factor, hTNFtg: human tumor necrosis factor  $\alpha$  transgenic mice, DA: Dark Agouti

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