

Euro
pain



Innovative Medicines Initiative

Finding a cure for chronic pain



IMI at the European Parliament - 6 October 2011



efpia

Chronic Pain – a widespread unmet clinical need



- 46,364 people surveyed across 16 Europe countries
- 19% (i.e. 75m in Europe) suffer Chronic pain (pain for at least 6 months duration, several times a week, Pain intensity >5/10)
- On average, sufferers live with chronic pain for 7 years (20% >20 years)
- One third reported that their pain was so severe they could not tolerate any more
- One in five reports losing a job or have been diagnosed with depression as a result of their pain
- 36% have inadequate pain control from medication



(www.painineurope.com)



Analgesic drugs listed in MIMS (Monthly Index of Medical Specialities)



Acunan

Diconal

Lodine

Pethidine

Medinol Paeditatric

Physeptone

Meptid

Ponstan



DHC continues

Lederfen

Paracetamol

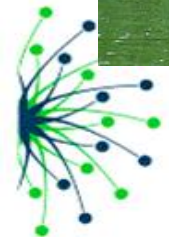
Zamadol SR

Paradote

Zomorph

Pentazocine

Zydol SR



Academic partners



London Pain Consortium (LPC)
David Bennett, (KCL),
Tony Dickenson, (UCL)
Stephen McMahon (KCL)
Kenji Okuse, (IC)
Christine Orengo (UCL)
Andrew Rice (IC),
Irene Tracey (Oxford)
John Wood (UCL).

German Pain Consortium (DFNS)
Thomas Tölle (Munich)
Rolf-Detlef Treede (Heidelberg)
Ralf Baron (Kiel)
Christoph Meier (Bochum)
Gerd Geisslinger (Frankfurt).

Spain
Jordi Serra
(SME)

Danish Pain Research Centre (DPRC)
Troels S. Jensen (Aarhus)
Henrik Kehlet (Copenhagen)
Søren Sindrup (Odense)
Nanna Finnerup (Aarhus)
Lene Vase (Aarhus).



EFPIA partners



- AstraZeneca AB, Sweden (*Project coordinator*)
- Boehringer Ingelheim International GmbH, Germany
- Pfizer Limited, Sandwich, UK – Wyeth Pharmaceuticals, USA
- Eli Lilly and Company Limited, United Kingdom
- Laboratorios del Dr Esteve SA, Spain
- UCB Pharma SA, Belgium
- Sanofi-Aventis Recherche & Developement, France
- Grunenthal, Germany
- Abbot (*subject to approval by IMI*)
- Astellas (*subject to approval by IMI*)



Studies in animals

1. Neurobiological mechanisms of chronic pain.

2. Improving animal models of pain

6. Identification of novel pain targets.

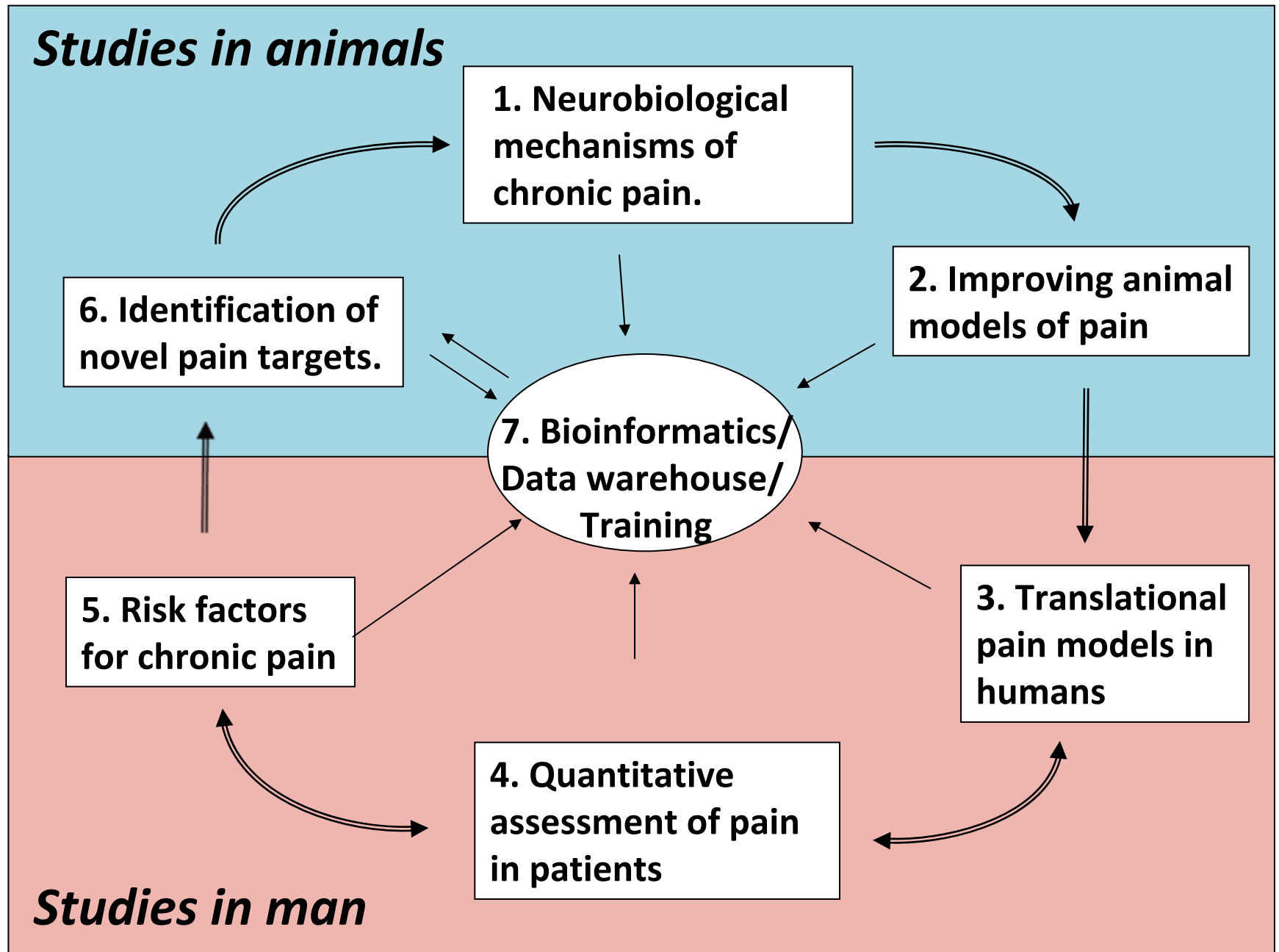
7. Bioinformatics/
Data warehouse/
Training

5. Risk factors for chronic pain

3. Translational pain models in humans

4. Quantitative assessment of pain in patients

Studies in man



Outcomes

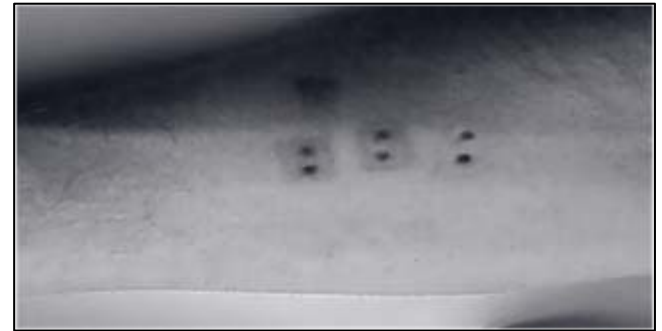


- 1) increase the understanding of chronic pain mechanisms;
- 2) facilitate the development of novel analgesic drugs;
- 3) improve the treatment of chronic pain patients.

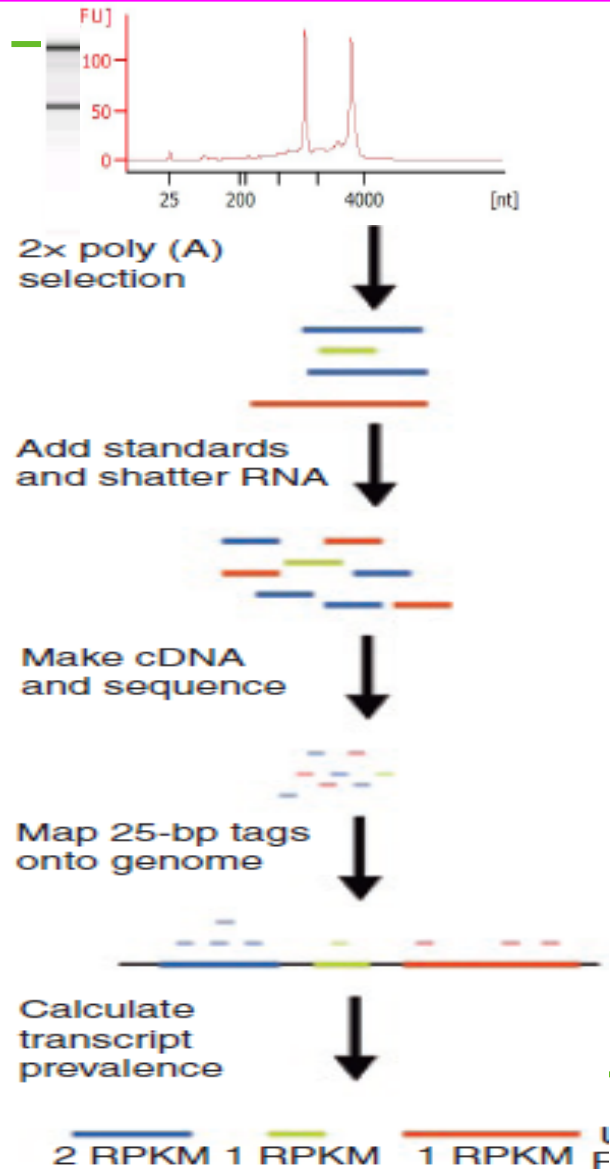
Start date: October 2009, 5 year funding



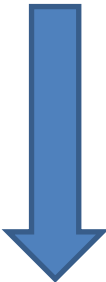
Finding new pain mediators



NEXT GENERATION RNA SEQUENCING



INPUT:
Total RNA



OUTPUT

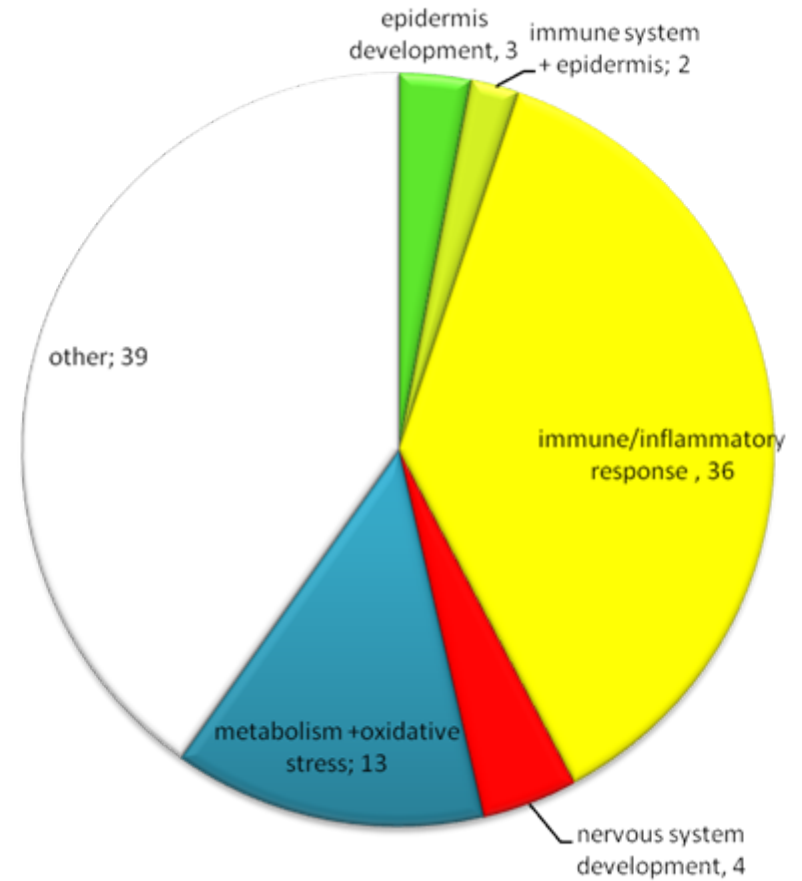
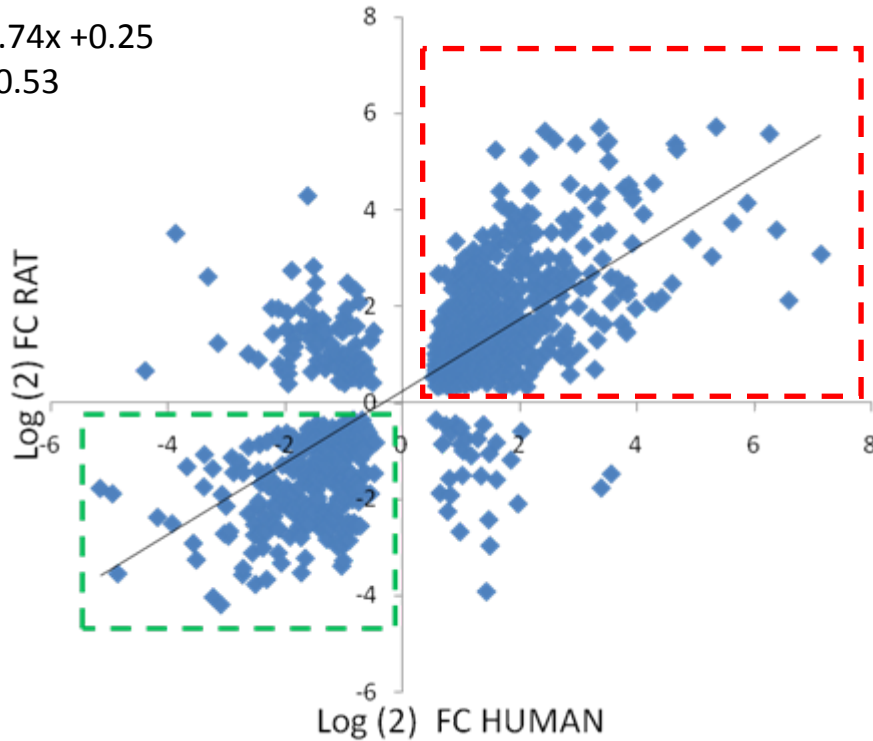
- ABSOLUTE QUANTIFICATION OF GENE EXPRESSION for DIFFERENTIAL GENE EXPRESSION
- EXON AND SPLICE JUNCTION READS
- NOVEL EXONS/SPLICE VARIANTS
- NOVEL GENES



Dysregulated Transcripts detected by Next Generation Sequencing in UVB



$y=0.74x+0.25$
 $R^2=0.53$



		HUMAN		
		DOWN	Not sig	UP
RAT	UP	97	2296	902
	n.s.	330	3393	314
	DOWN	330	848	32

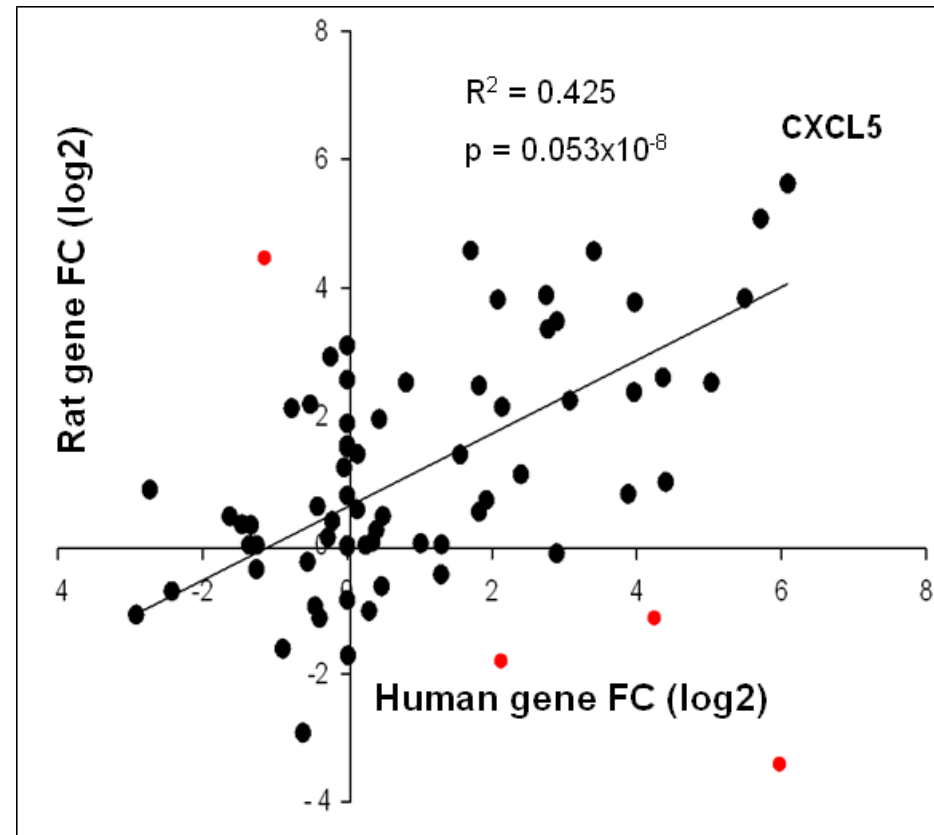
(n= 8542 orthologues assigned)



Inflammatory mediators are positively correlated between the human and the rat



GENE	HUMAN	RAT
CXCL5	68.0 (52.6-87.8)	49.4 (34.2-71.2)
IL-24	52.5 (45.5-60.5)	33.7 (20.0-56.7)
IL-6	45.1 (35.3-57.5)	14.3 (8.6-23.7)
G-CSF	20.6 (14.5-29.1)	6.1 (2.7-13.5)
CXCL2	10.6 (8.8-12.8)	23.8 (11.3-45)
CCL3	32.7 (26.8-40.0)	5.8 (3.7-8.9)
CXCL1	15.6 (12.7-19.0)	5.2 (3.5-7.9)
IL-10	6.8 (5.4-8.6)	10.3 (7.6-14)
CCL7	15.7 (12-20.7)	13.7 (9.6-19.5)
CCL4	6.7 (5.2-8.7)	14.8 (10.7-20.5)
CCL2	4.2 (3.6-5.0)	14.1 (9.4-21.2)
CCL11	7.4 (6.1-9.1)	11.2 (8.2-15.2)
IL-1beta	8.4 (6.6-10.8)	4.8 (3.0-7.9)
COX-2	4.4 (3.4-5.6)	4.4 (3.2-6.1)

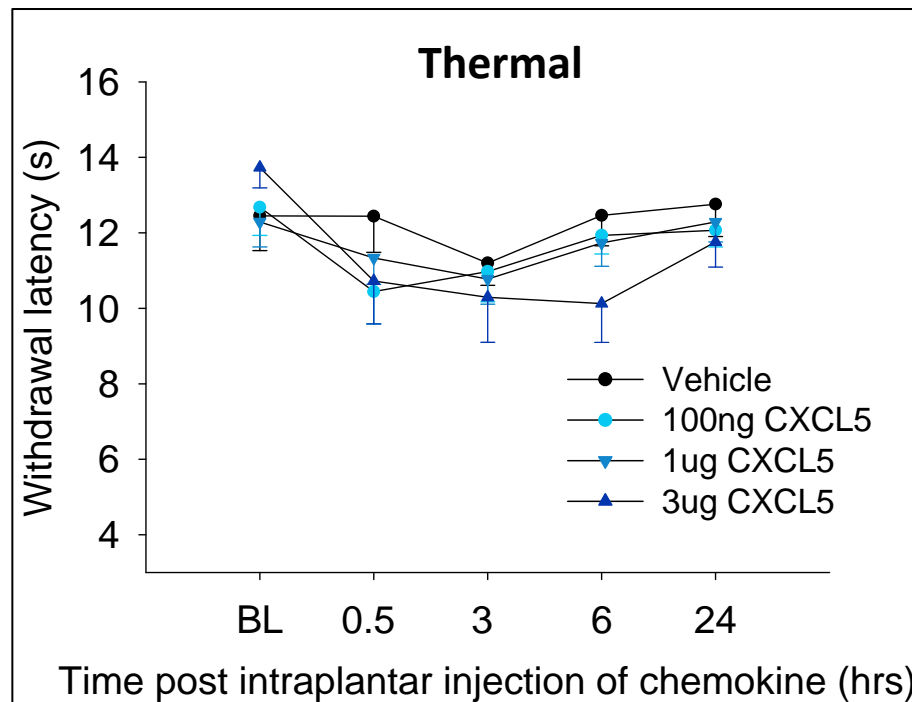
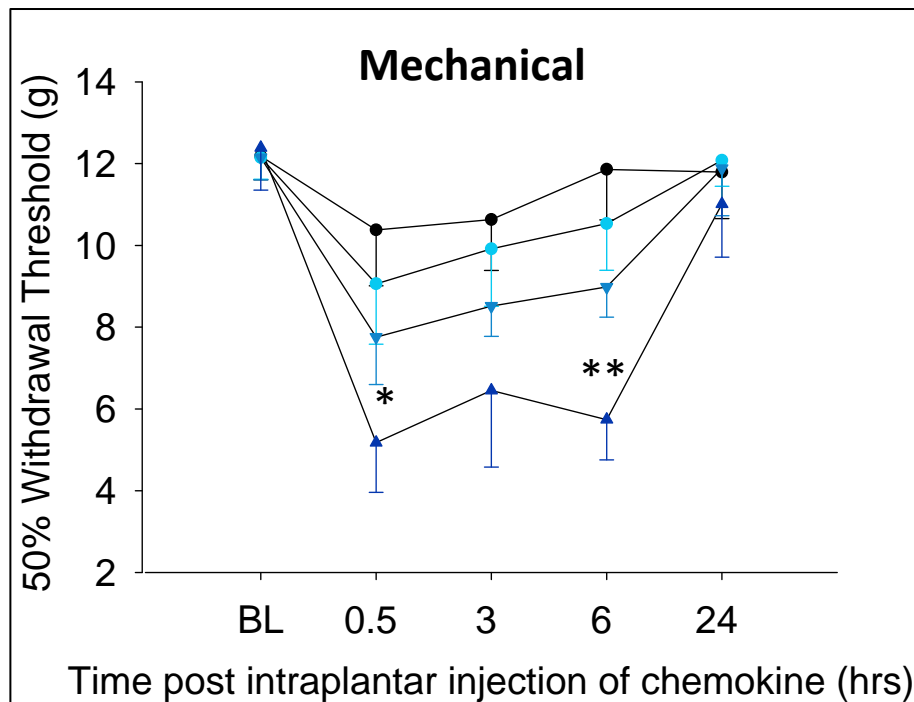


Science Transl Med 3, 90ra60 (2011)

Normalised to GAPDH. Mean FC
(UV/Control) \pm SEM



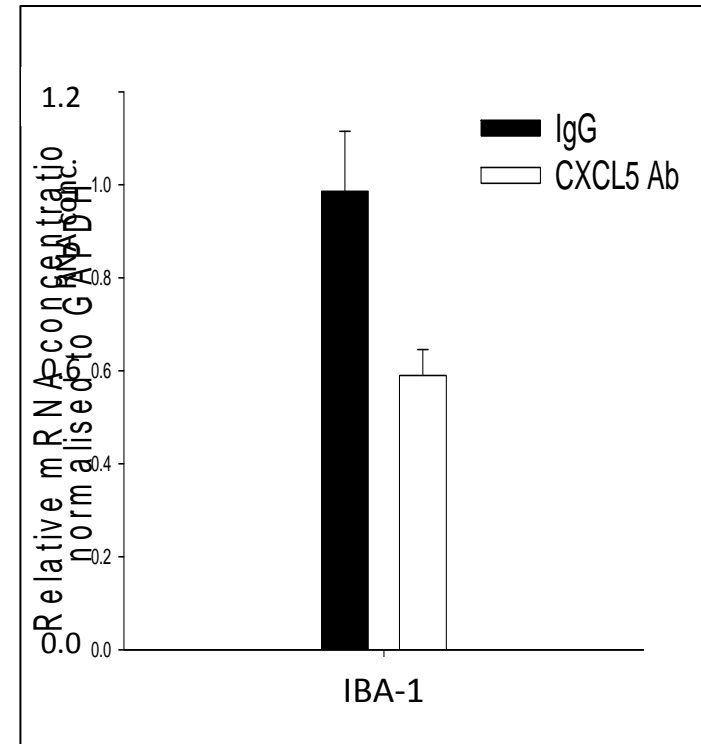
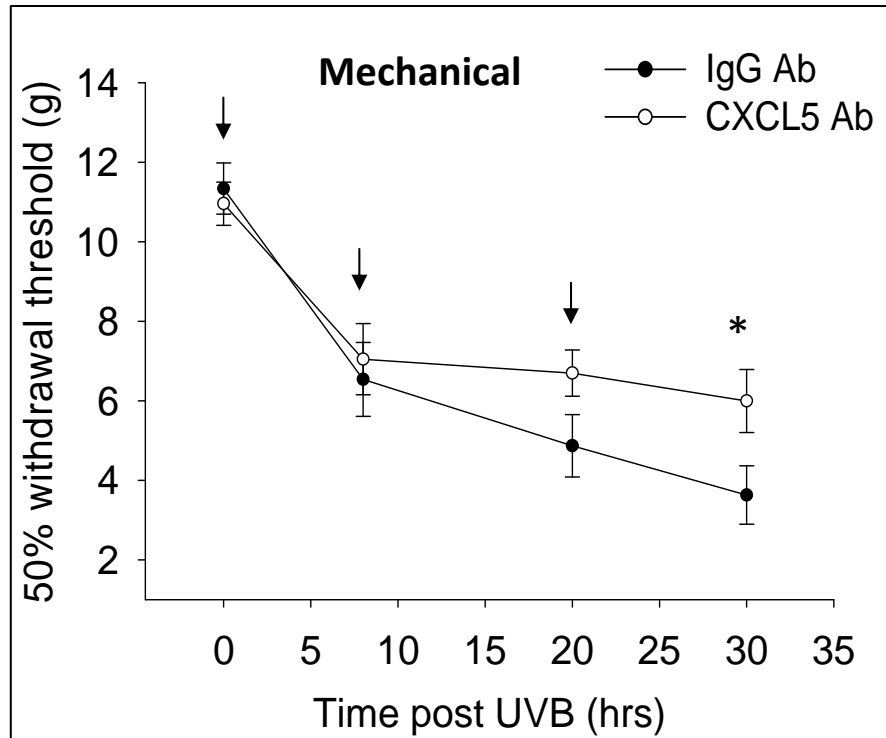
CXCL5 induces dose dependent mechanical pain related hypersensitivity in the rat



Neutralisation of endogenous CXCL5 attenuates UVB induced mechanical hypersensitivity



Science Translational Medicine 3, 90ra60 (2011)



Cumulative doses of neutralising Ab; 10 μ g injected intra-plantar. n=11



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Studies in man

Further information



- Academic lead: Stephen.McMahon@kcl.ac.uk
- EFPIA lead: Marta.Segerdahl@astrazeneca.com
- URL: under construction, link at www.lpc.ac.uk
 - Admin support: Maritha.X.Karlsson@astrazeneca.com
 - Press Release at
- http://www.kcl.ac.uk/news/news_details.php?news_id=1342&year=2010

www.imi.europa.eu

