Process to developing therapies to prevent the acute to chronic pain transition - What is needed? Preclinical Perspective

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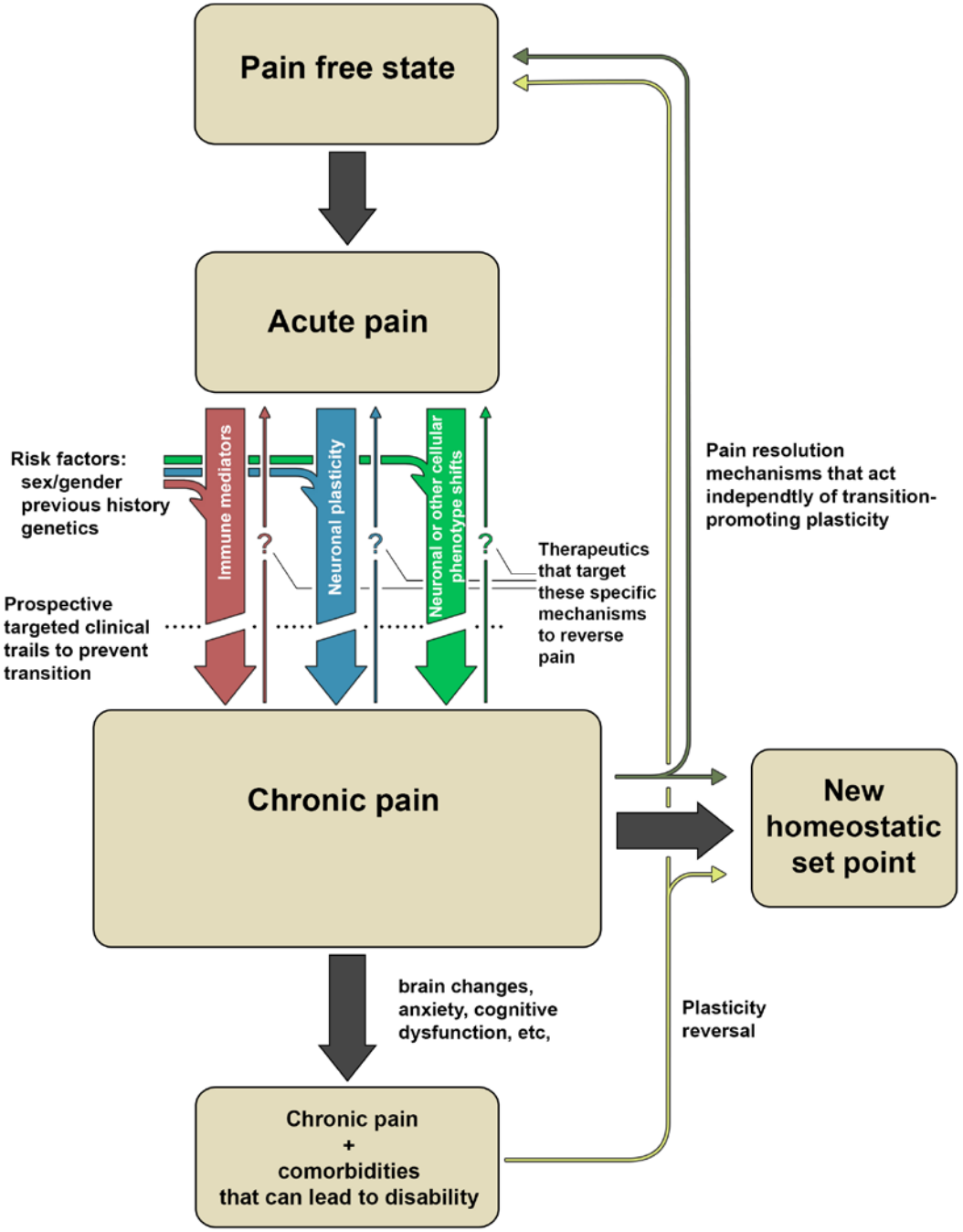
CerSci



What is the transition from acute to chronic pain?

A plasticity driven event that persistently alters the responsiveness of the pain system

What do preclinical models tell us about preventing the transition to chronic pain?

Our current best acute pain medicine may promote mechanisms that facilitate the transition to chronic pain

We have to develop acute pain medicines that also prevent this transition

nature neuroscience

Morphine hyperalgesia gated through microglia-mediated disruption of neuronal Cl^- homeostasis

Francesco Ferrini[1–3,10], Tuan Trang[4–7,10], Theresa-Alexandra M Mattioli[8], Sophie Laffray[1,2], Thomas Del'Guidice[1,2], Louis-Etienne Lorenzo[1,2], Annie Castonguay[1,2], Nicolas Doyon[1,2], Wenbo Zhang[4,5], Antoine G Godin[1,2], Daniela Mohr[4,5], Simon Beggs[4,5], Karen Vandal[1], Jean-Martin Beaulieu[1,2], Catherine M Cahill[8,9], Michael W Salter[4,5] & Yves De Koninck[1,2]

nature medicine

Blocking microglial pannexin-1 channels alleviates morphine withdrawal in rodents

Nicole E Burma[1,2], Robert P Bonin[3], Heather Leduc-Pessah[1,2], Corey Baimel[2], Zoe F Cairncross[1,2], Michael Mousseau[1,2], Jhenkruthi Vijaya Shankara[4], Patrick L Stemkowski[2], Dinara Baimoukhametova[2], Jaideep S Bains[2], Michael C Antle[2,4], Gerald W Zamponi[2], Catherine M Cahill[5], Stephanie L Borgland[2], Yves DeKoninck[6] & Tuan Trang[1,2]

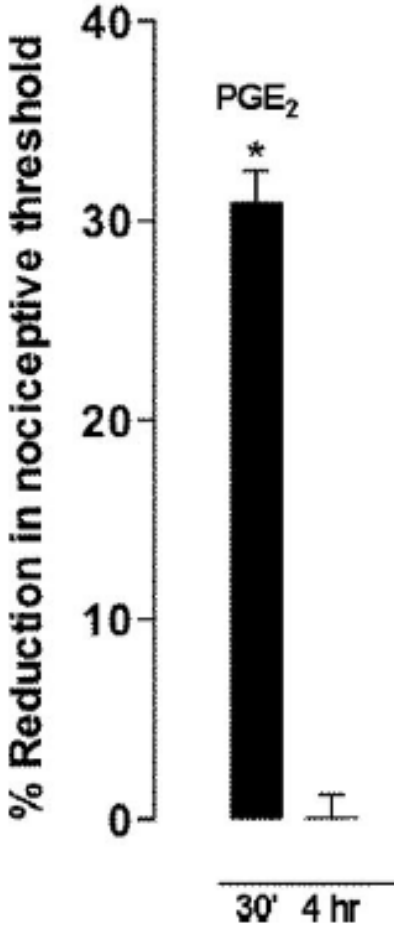
Cellular/Molecular

Shared Mechanisms for Opioid Tolerance and a Transition to Chronic Pain

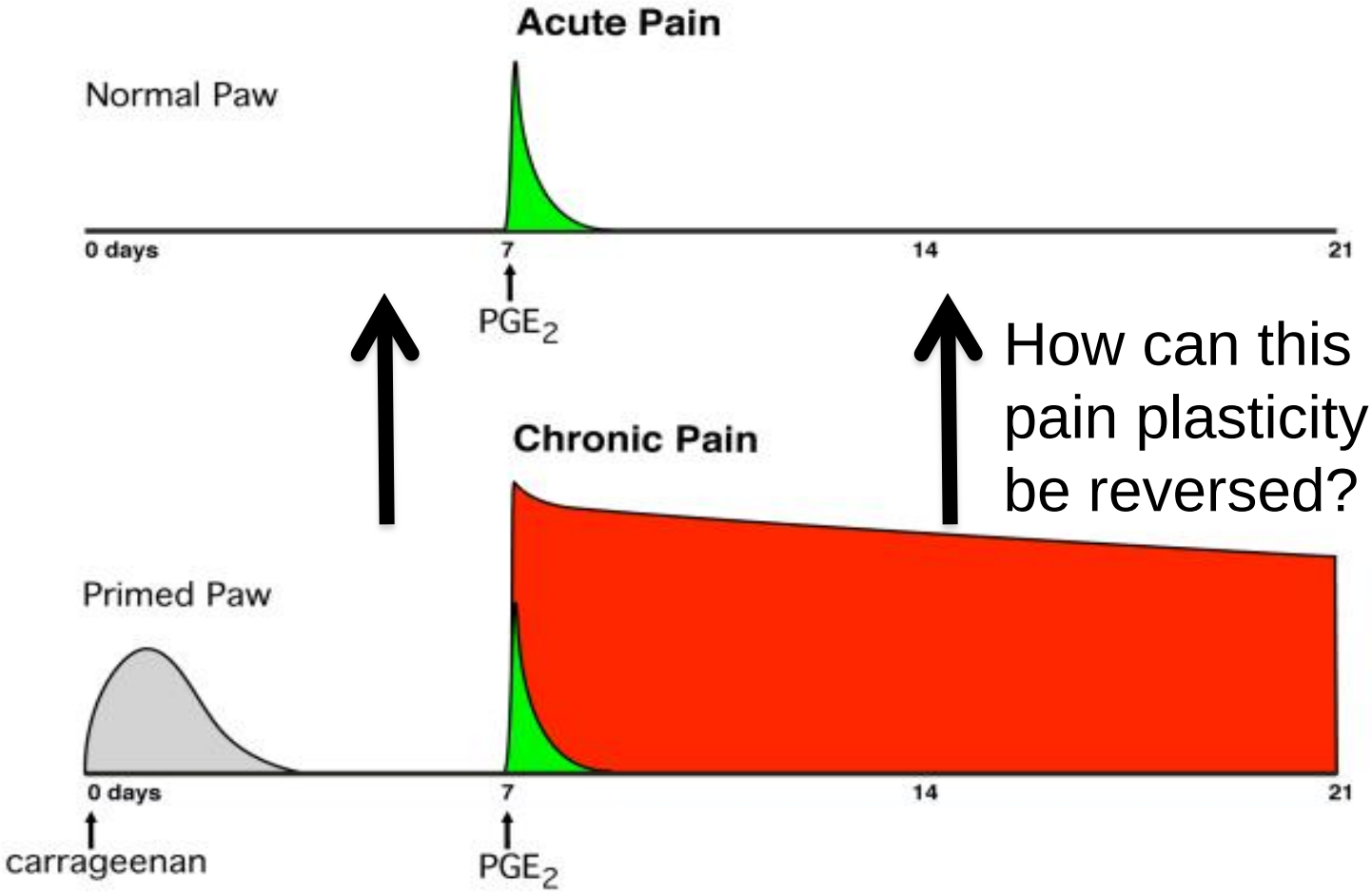
Elizabeth K. Joseph, David B. Reichling, and Jon D. Levine
Departments of Medicine and Oral Surgery, Division of Neuroscience, University of California, San Francisco, San Francisco, California 94143-0440

3) But repeated mu-opioid stimulation causes a loss of efficacy and exacerbates PGE2 effect

1) PGE2 produces a transient hypersensitivity

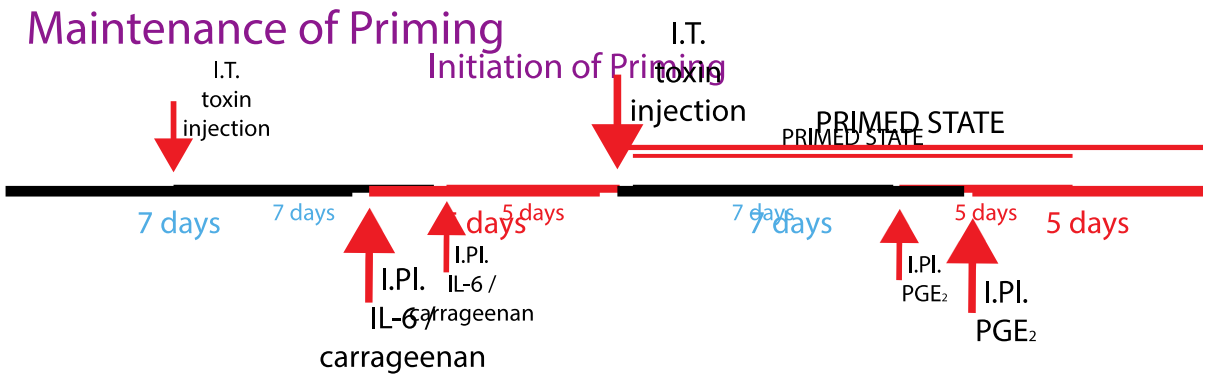


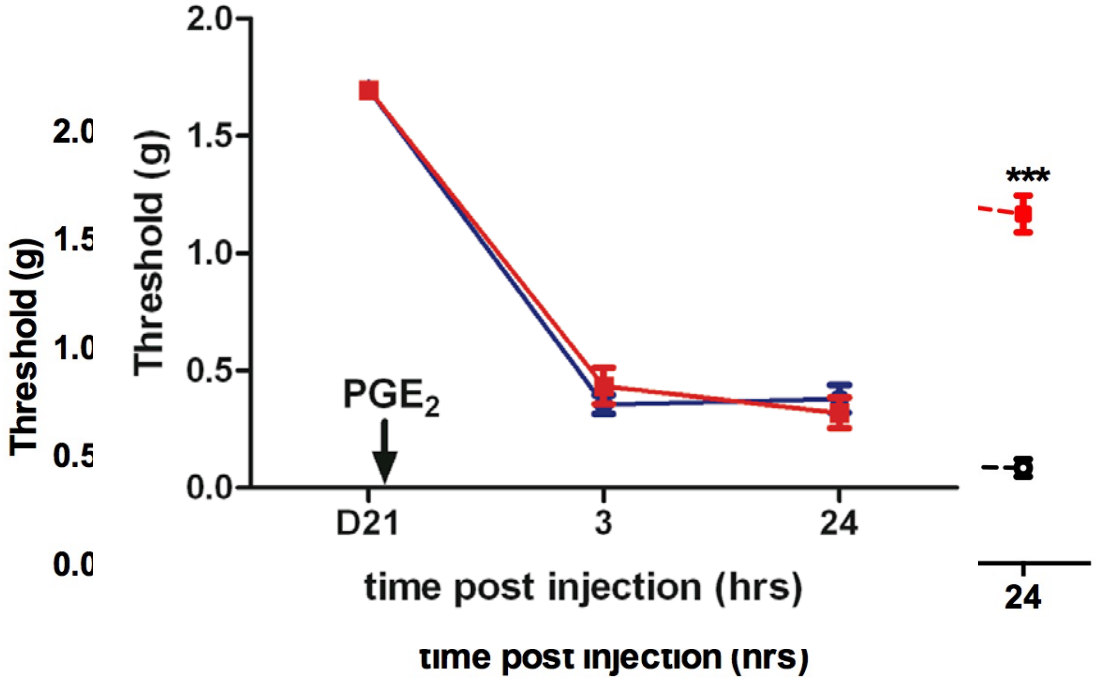
Hyperalgesic Priming as a Model of the Chronic Pain Transition



Reichling and Levine, Trends in Neurosciences (2009)

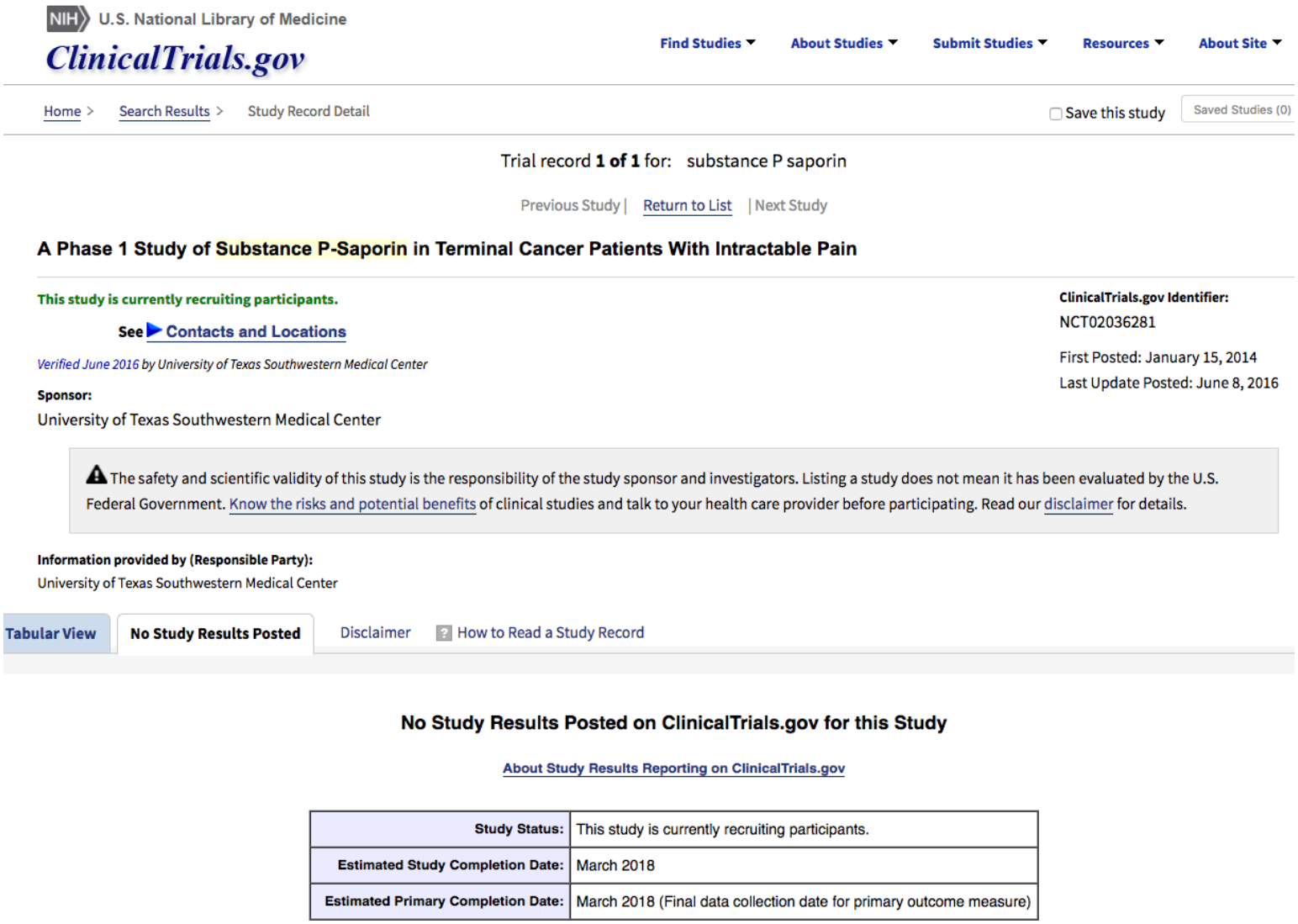
Hyperalgesic Priming as a Model of the Chronic Pain Transition: Changes in neural circuitry in the transition to chronic pain?





Ji-Young Kim, Journal of Neuroscience 2015

The NK-1 ablation hypothesis is being tested in humans – preclinical model would predict a lack of efficacy (tragically)



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Trial record **1 of 1** for: substance P saporin

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A Phase 1 Study of Substance P-Saporin in Terminal Cancer Patients With Intractable Pain

This study is currently recruiting participants.

See Contacts and Locations

Verified June 2016 by University of Texas Southwestern Medical Center

Sponsor:
University of Texas Southwestern Medical Center

ClinicalTrials.gov Identifier:
NCT02036281

First Posted: January 15, 2014
Last Update Posted: June 8, 2016

⚠ The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Information provided by (Responsible Party):
University of Texas Southwestern Medical Center

Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

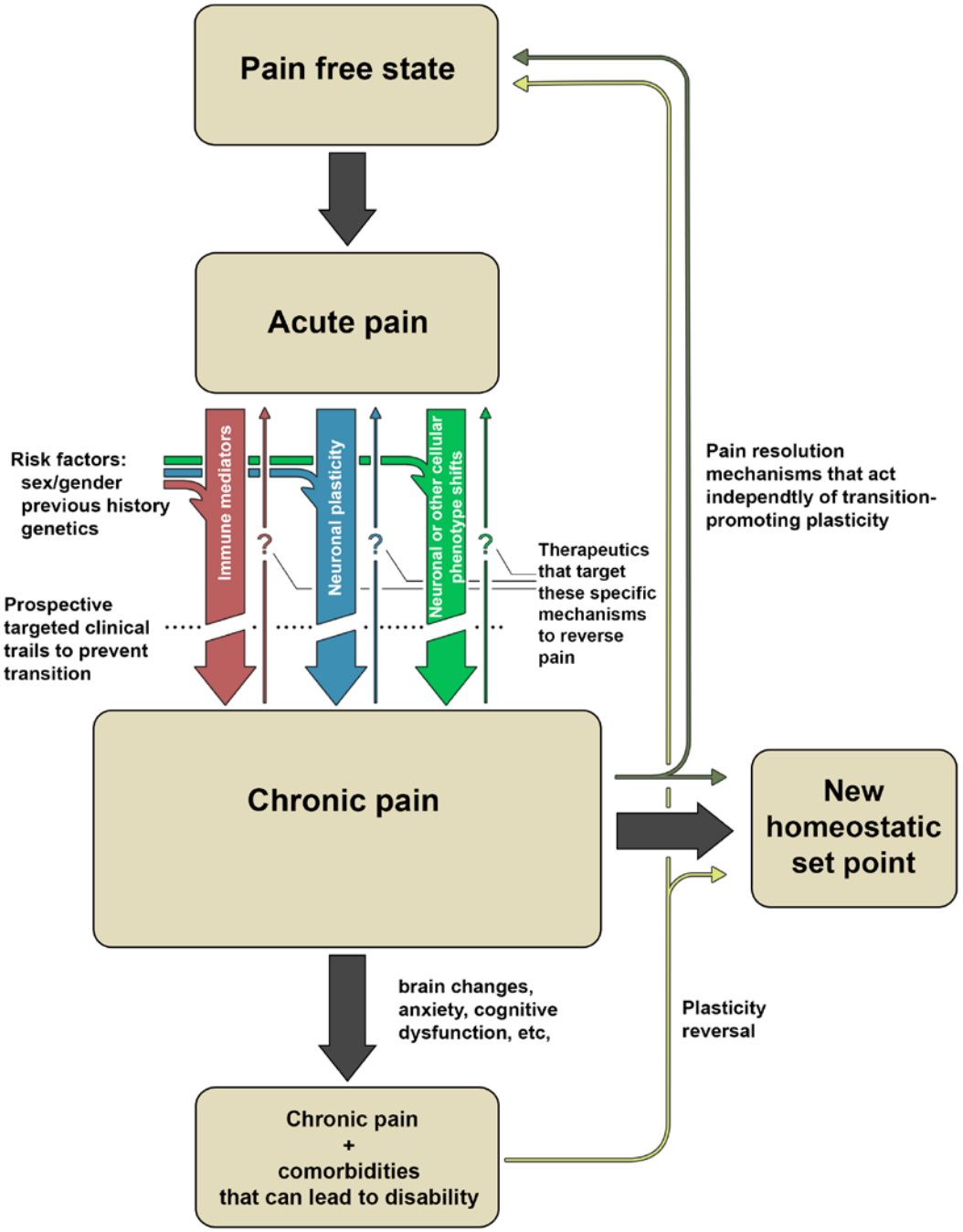
No Study Results Posted on ClinicalTrials.gov for this Study

About Study Results Reporting on ClinicalTrials.gov

Study Status:	This study is currently recruiting participants.
Estimated Study Completion Date:	March 2018
Estimated Primary Completion Date:	March 2018 (Final data collection date for primary outcome measure)

Advantages of “priming” or ”latent sensitization” models

- Possibility of identifying neural circuits that differentially contribute to acute and chronic pain (e.g. dopamine in the brain – Apkarian - and spinal cord - Price)
- Already described that many analgesics that are ineffective in humans with chronic pain are ineffective in primed animals.
- Possibility to accurately predict whether an acute treatment can prevent the transition to chronic pain/priming



Can we reverse the transition from acute to chronic pain?

New emphasis on pain resolution mechanisms as an important area of discovery for next generation therapeutics

A few ideas on chronic pain resolution mechanisms

The resolvin hypothesis

nature medicine

Resolvins RvE1 and RvD1 attenuate inflammatory pain via central and peripheral actions

Zhen-Zhong Xu[1,3], Ling Zhang[1,3], Tong Liu[1], Jong Yeon Park[1], Temugin Berta[1], Rong Yang[2], Charles N Serhan[2,3] & Ru-Rong Ji[1,3]

The AMPK activation hypothesis

RESEARCH Open Access

Targeting adenosine monophosphate-activated protein kinase (AMPK) in preclinical models reveals a potential mechanism for the treatment of neuropathic pain

Ohannes K Melemedjian[1], Marina N Asiedu[1], Dipti V Tillu[1], Raul Sanoja[1], Jin Yan[1], Arianna Lark[1], Arkady Khoutorsky[2,3], Jessica Johnson[1], Katherine A Peebles[1], Talya Lepow[1], Nahum Sonenberg[2,3], Gregory Dussor[1,4] and Theodore J Price[1,4,5*]

The IL-10 immune modulator hypothesis

Neurobiology of Disease

IL4-10 Fusion Protein Is a Novel Drug to Treat Persistent Inflammatory Pain

Niels Eijkelkamp,[1,2] Cristine Steen-Louws,[1] Sarita A. Y. Hartgring,[1] Hanneke L. D. M. Willemen,[2] Judith Prado,[1] Floris P. J. G. Lafeber,[3] Cobi J. Heijnen,[4] C. E. Hack,[1] Joel A. G. van Roon,[1*] and Annemieke Kavelaars[4*]
Laboratories of [1]Translational Immunology and [2]Neuroimmunology and Developmental Origins of Disease and [3]Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, 3584 EA Utrecht, The Netherlands, and [4]Neuroimmunology Laboratory, Department of Symptom Research, MD Anderson Cancer Center, University of Texas, Houston, Texas 77030

Behavioral/Cognitive

$CD8^+$ T Cells and Endogenous IL-10 Are Required for Resolution of Chemotherapy-Induced Neuropathic Pain

Karen Krukowski,[1] Niels Eijkelkamp,[3,4*] Geoffroy Laumet,[1*] C. Erik Hack,[3] Yan Li,[2] Patrick M. Dougherty,[2] Cobi J. Heijnen,[1] and Annemieke Kavelaars[1]
[1]Laboratory of Neuroimmunology, Division of Internal Medicine, and [2]Department of Anesthesiology and Pain Medicine Research, The University of Texas MD Anderson Cancer Center, Houston, Texas 77030, and [3]Laboratory of Translational Immunology, and [4]Laboratory of Neuroimmunology and Developmental Origins of Disease, University Medical Center Utrecht, 3584EA Utrecht, The Netherlands

Research Paper

PAIN

Prior voluntary wheel running attenuates neuropathic pain

Peter M. Grace[a,b,c,*], Timothy J. Fabisiak[a,b], Suzanne M. Green-Fulgham[a,b], Nathan D. Anderson[a,b], Keith A. Strand[a,b], Andrew J. Kwilasz[a,b], Erika L. Galer[a,b], Frederick Rohan Walker[d], Benjamin N. Greenwood[b,e], Steven F. Maier[a,b], Monika Fleshner[b,e], Linda R. Watkins[a,b]