



JAK Inhibitors for Chronic Itch: What's the Future?



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SCHOOL OF MEDICINE



Disclosures

- Consultant
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- Advisory Board
 - Cara, Kiniksa, Menlo
- Stockholder
 - Locus Biosciences
- Founder and Chief Scientific Officer
 - Nuogen Pharma, Inc.
- Patents
 - Patent pending for JAK inhibitors in chronic itch



What is chronic pruritus or itch?

Itch

1. an uncomfortable sensation on the skin that causes a desire to scratch

Chronic itch

1. itch that lasts for longer than six weeks



The problem and unmet need

1. Chronic itch affects $>15\%$ of the population
2. Negative impact on quality of life comparable to chronic pain
3. Incidence is increasing
4. No FDA-approved medications



Itch may be the most common medical symptom

- Dermatologic
 - **Atopic dermatitis (AD)**, contact dermatitis, lichen planus, prurigo nodularis, psoriasis
- Infection
 - HIV, mites/parasites
- Malignancy
 - Polycythemia vera, leukemia, lymphoma
- Medication-induced
 - Opioids, checkpoint inhibitors
- Neurologic
 - Shingles, disc herniation, multiple sclerosis
- Systemic
 - Thyroid, kidney, and liver disease
- Idiopathic
 - **Chronic pruritus of unknown origin (CPUO)**



The opportunity in chronic itch

1. Accessible population of 19 million in U.S.
2. \$5.4 billion market in U.S.
3. Large population of discouraged patients
4. Recent discovery of itch-specific pathways



JAK inhibitors are rapidly emerging for the treatment of atopic dermatitis

CONFERENCE COVERAGE

JAK inhibitors for atopic dermatitis might hit JAK-pot

Publish date: December 12, 2017

By [Bruce Jancin](#)

Internal Medicine News.

CONFERENCE COVERAGE

Novel topical JAK inhibitor shows promise for atopic dermatitis

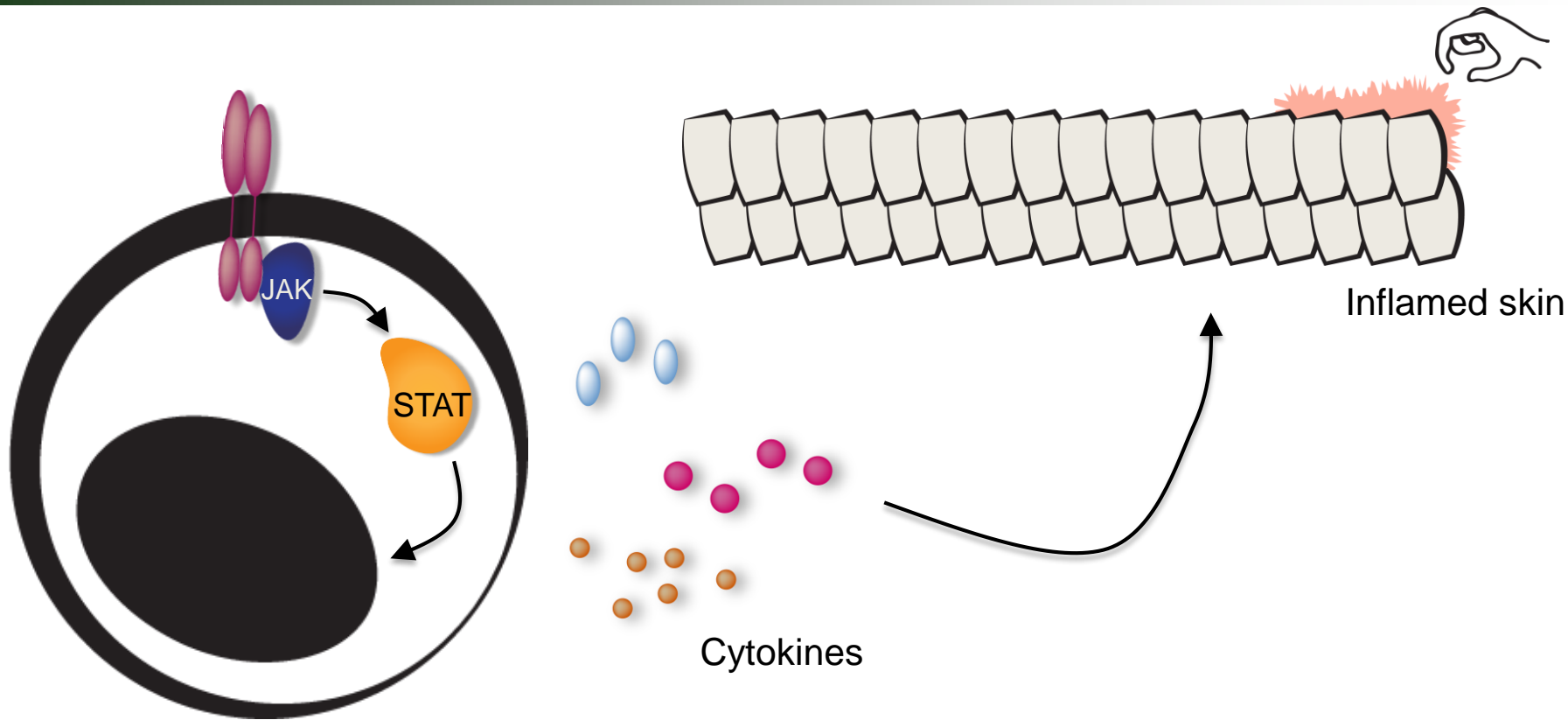
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By [Bruce Jancin](#)

Internal Medicine News.



The immunologic paradigm of JAK-STAT signaling





Companies boldly entering the itch therapeutic space

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CARA
THERAPEUTICS

About Therapeutic Focus Pipeline

sienna
biopharmaceuticals



Menlo Therapeutics

HOME

VANDA
PHARMACEUTICALS INC.

Menlo Therapeutics Inc. is a late stage biopharmaceutical company focused on the development of serlopitant for the treatment of pruritus (itch) associated with dermatologic conditions such as atopic dermatitis, psoriasis and prurigo nodularis, and for refractory chronic cough.



Itch-sensory neurons employ JAKs

Article

Cell

Sensory Neurons Co-opt Classical Immune Signaling Pathways to Mediate Chronic Itch

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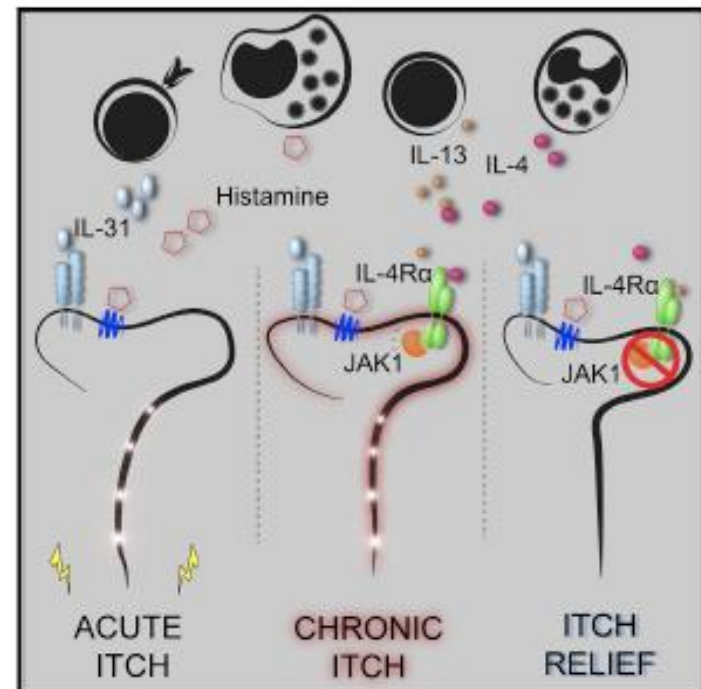
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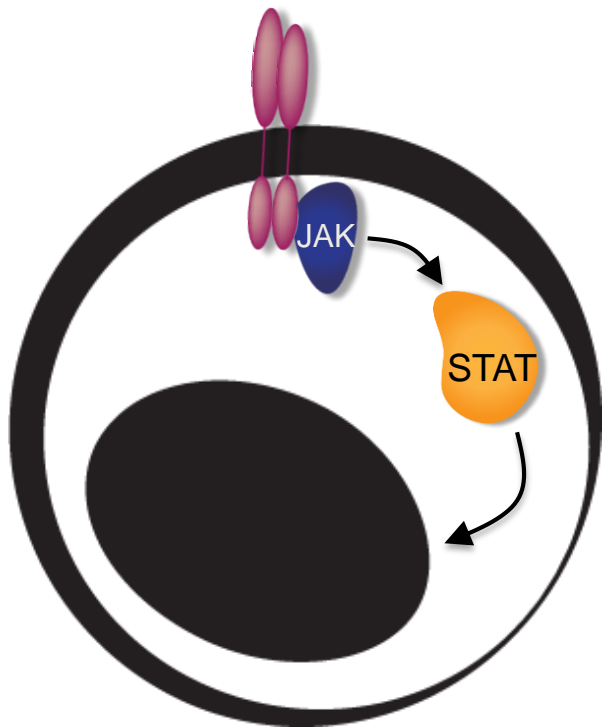
<http://dx.doi.org/10.1016/j.cell.2017.08.006>



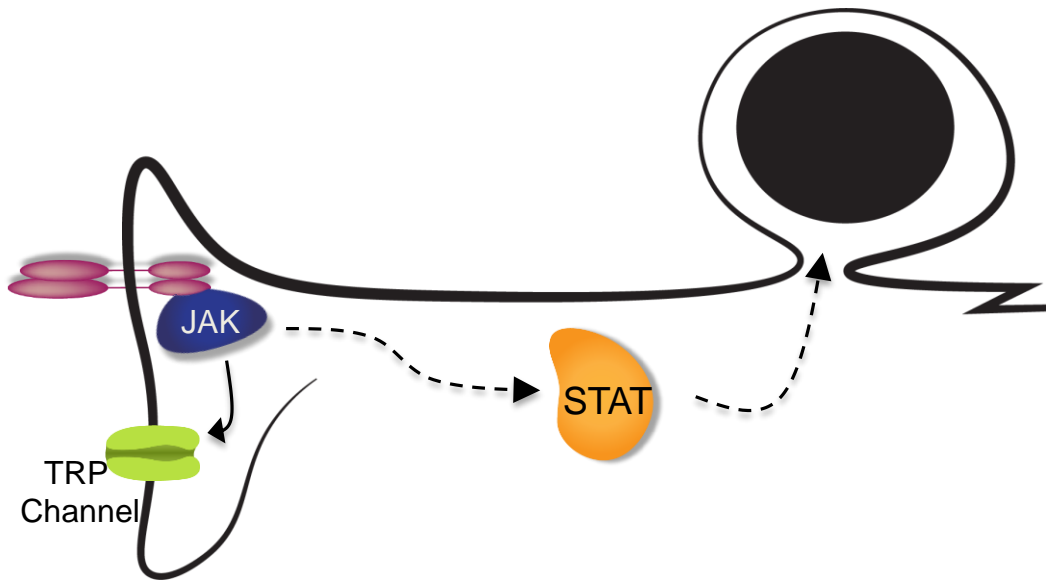


The sensory paradigm of JAK-STAT signaling

Immune Cell



Sensory Neuron





Oral JAK inhibitors have itch-selective effects



| PRESSROOM (/)

SEPTEMBER 7, 2017

AbbVie's Upadacitinib (ABT-494) Meets Primary
Endpoint in Phase 2b Study in Atopic Dermatitis

- Upadacitinib demonstrated reduction in pruritus (itch) within the first week and improvement in skin within the first two weeks for all doses[1]

- Study shows positive results for upadacitinib and no new safety signals detected[1]
- All doses achieved the primary endpoint of greater mean percentage change from baseline in Eczema Area and Severity Index (EASI) score versus placebo at 16 weeks[1]
- Clear or almost clear skin was achieved by 50 percent of patients receiving 30 mg once-daily dose of upadacitinib[1]
- Upadacitinib demonstrated reduction in pruritus (itch) within the first week and improvement in skin within the first two weeks for all doses[1]
- Upadacitinib, an oral agent engineered by AbbVie to selectively inhibit JAK1, is being studied as a once-a-day therapy in atopic dermatitis and across multiple immune-mediated diseases[2],[3],[4-9]



Oral JAK inhibitors have itch-selective effects

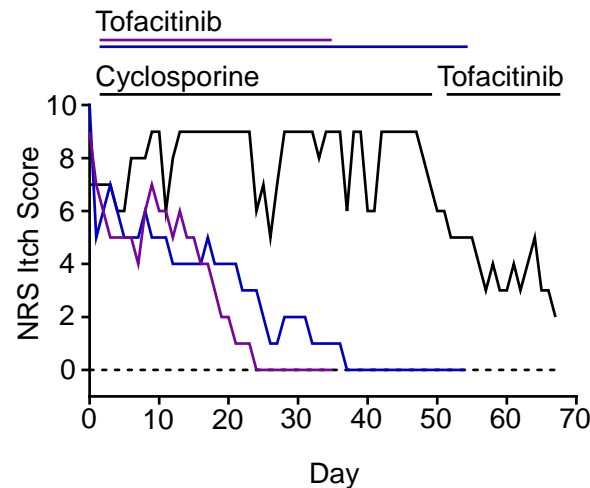
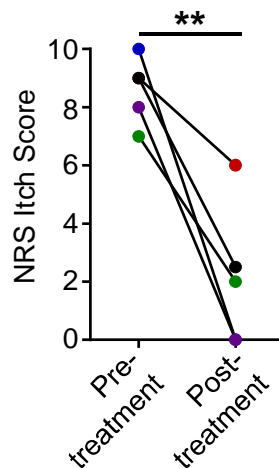
Atopic Dermatitis



Chronic Pruritus of Unknown Origin (CPUO)



Chronic Pruritus of Unknown Origin (CPUO)





Topical JAK inhibitors demonstrate anti-itch effects by 24-36 hours

CLINICAL TRI

**Topical
randomi**

R. Bissonnette,
C. Mamolo,⁷ J.

A Phase 2, Randomized, Dose-Ranging, Vehicle- and Active-Controlled Study to Evaluate the Safety and Efficacy of Ruxolitinib Cream in Adult Patients With Atopic Dermatitis

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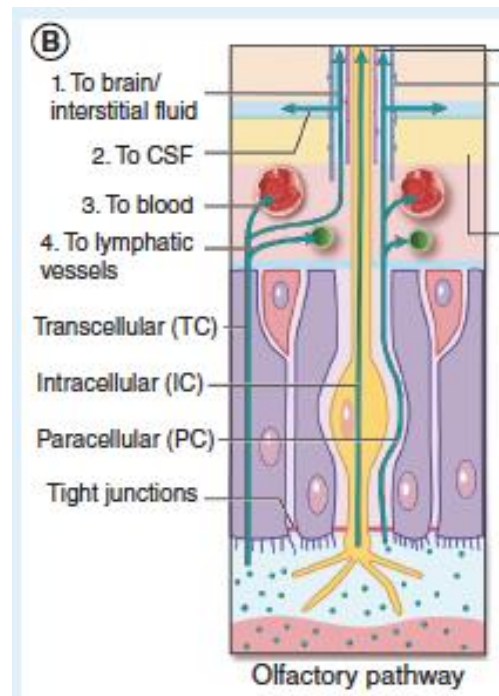
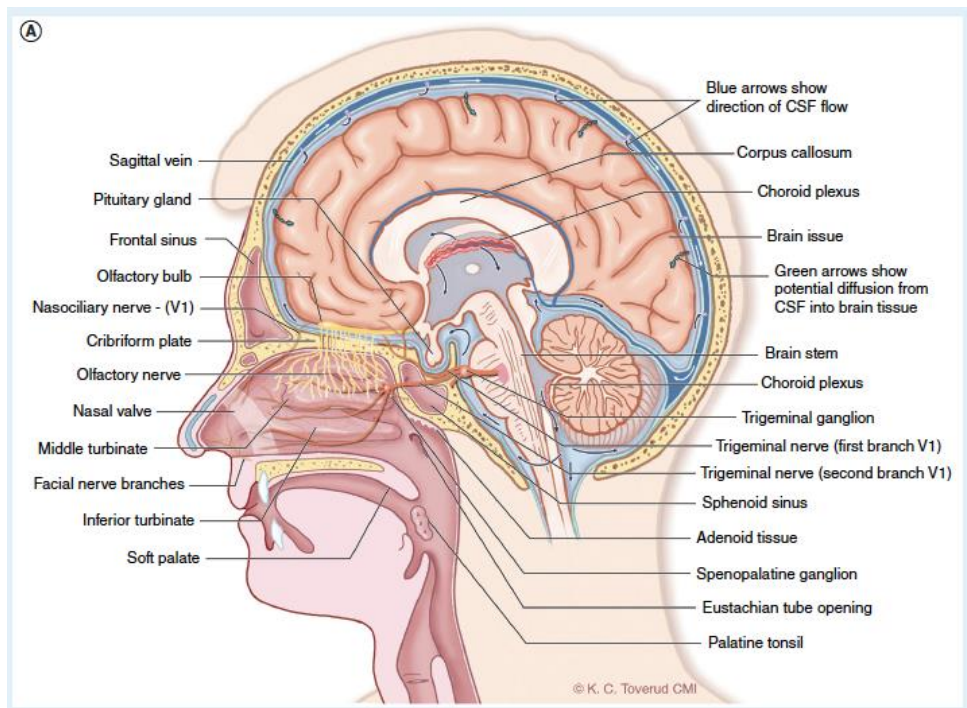
BJD
Journal of Dermatology

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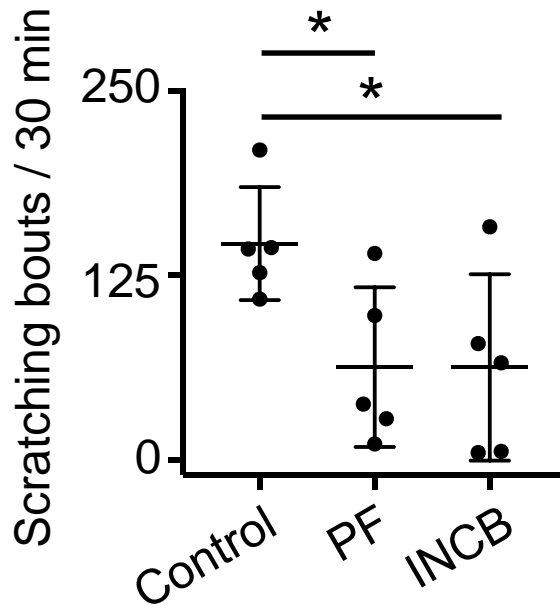
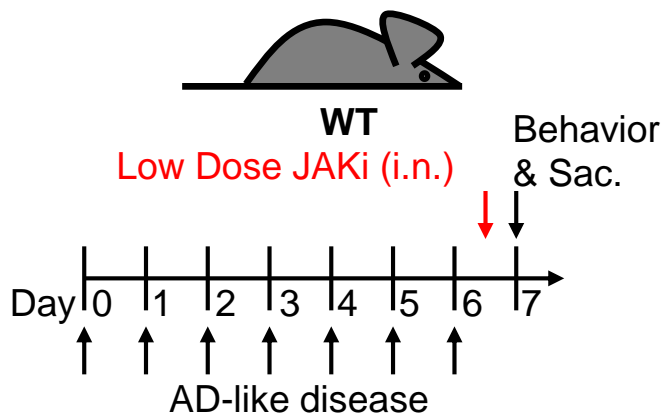


The intranasal route can directly access the cerebrospinal fluid





Intranasal JAK inhibition suppresses itch



JAK1-selective Inhibitors:
PF – PF-04965842
INCB – itacitinib

*P value = 0.0417
Ordinary one-way ANOVA



Chronic itch beyond atopic dermatitis

Chronic Pruritus of Unknown Origin

Idiopathic
Elderly pruritus



Malignancy-Associated Pruritus

Leukemia/lymphoma
Polycythemia vera

Neuropathic Pruritus

Brachioradial pruritus
Notalgia paresthetica
Scalp pruritus
Genital pruritus

Medication-Associated Pruritus

Opioids
Checkpoint inhibitors

Systemic Pruritus

Chronic kidney disease
Hepatobiliary disease



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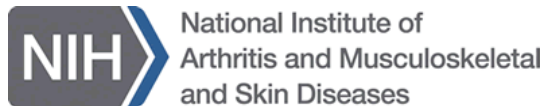
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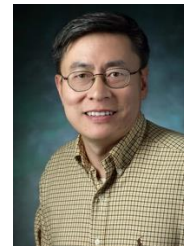
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