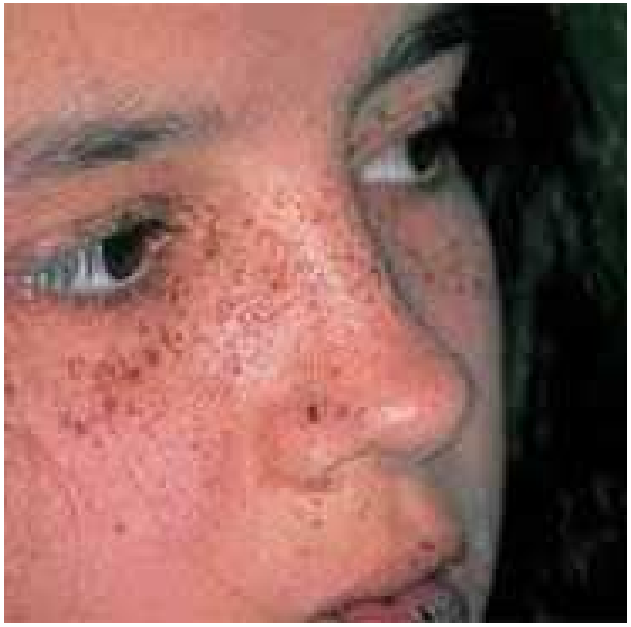
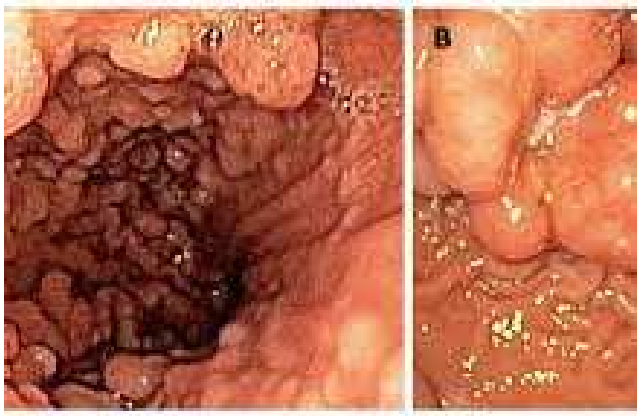




PJS Treatment: Master Tumor Suppressor LKB1/STK11

Polyposis treatment and potential chemo prevention

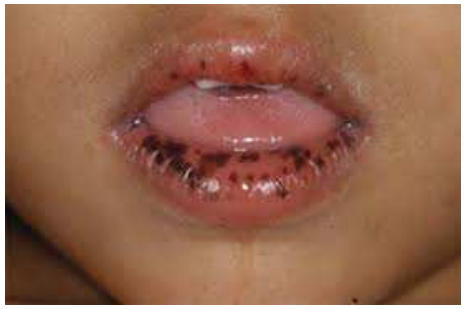
- **Peutz-Jeghers Syndrome (PJS)** is a cancer pre-disposition disorder and a polyposis syndrome.
- PJS places 93% increased risk of developing cancer throughout lifespan.
- Mutation of STK11/LKB1 master tumor suppression gene, either germline or somatic increases risk of cancer globally. 50% of PJS cases are de novo (no family history).
- Associated cancers include but are not limited to cancers of the: lung, breast, colon, pancreatic, esophagus, stomach, ovaries, cervix, testicles and gastrointestinal tract.
- Currently, only treatment model is invasive screening and surgical polyp/tumor removal every 6-24 months.
- An estimated 1:25,000 to 300,000 people may have PJS. PJS's hidden symptoms make diagnosis very challenging.
- FDA and EMA approved ruxolitinib has therapeutic potential in PJS.
- Treatment of LKB1 deficient mice with the JAK1/2 inhibitor ruxolitinib dramatically decreased polyposis. Validation has also been confirmed with human tissues.
- Next step is to move to request fast tracking to human trials with ruxolitinib in diagnosed patients and repurpose ruxolitinib for PJS.

Peutz-Jeghers Syndrome

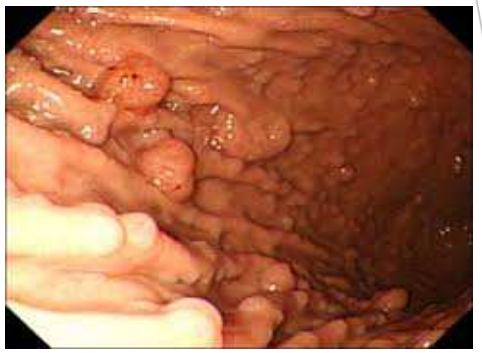
Urgent Help!

"I am searching for anyone who has had to have their stomach removed because I was told my **stomach should be removed** due to it being covered with polyps."

"My **5-year-old** has PJS, had 2 colonoscopies so far within 6 months period due to blood in his stool. They removed 8 Polyps!"

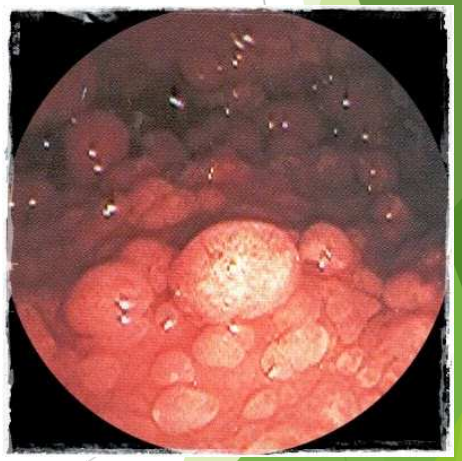


"Pill cam that I had this past June showed over **100 polyps!!!"**



"I just had the results for my son's MRI (9years old). They found polyps very far inside small intestine and colon. The **GI doctor is afraid.**"

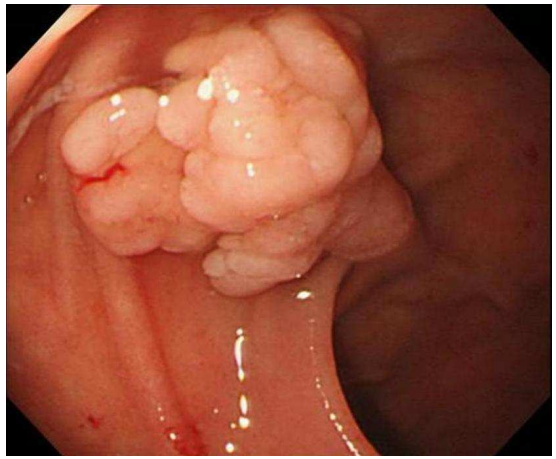
"Just wondering if any of you have a child who has refused medical treatment due to **fear/trauma!"**



"My daughter had **intussusceptions** at age 3 and 10. Both times resulted in bowel resections. At the time of her first surgery, they also removed her appendix. She also has had painful and irregular menstrual cycles."

"My father, son, daughter and myself all have PJS. My father had Rheumatic fever as a child, an intussusception in his 20s and **died at age of 40** from pancreatic cancer that spread to his liver and lung!"

Peutz-Jeghers Syndrome

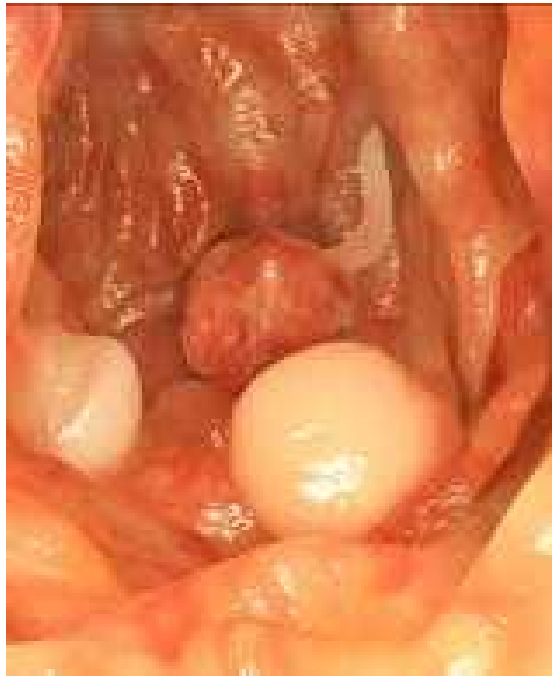


What is Peutz-Jeghers Syndrome (PJS)?

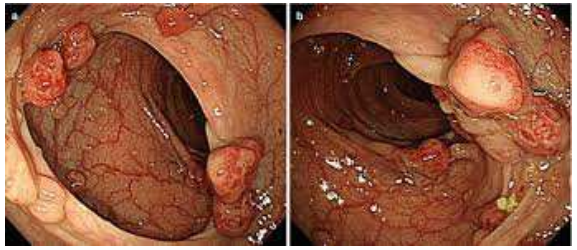
- Chronic disease caused by mutation of STK11/LKB1 master tumor suppressor gene.
- Master tumor suppressor mutation leads to uncontrollable growth and proliferation of cells which result in polyps/tumors that may lead to cancer, along with independent cancers globally.
- May be acquired (de novo) or hereditary (a parent diagnosed with PJS has a 50% chance of passing the gene to their children).
- Current standard of care for patients who are aware of having PJS has been to “wait and see” and to treat as symptoms appear, many with years of misdiagnosis and procedures.
- PJS also presents hidden symptoms so many affected are not even aware they have PJS until later years when they are suddenly faced with emergency situations, if not already too late!

93% increased risk of Cancer!

PJS: Polyposis Syndrome



- Polyps cause bowel obstruction, chronic sudden bleeding, anemia, vomiting, abdominal pain and intussusception requiring emergency surgical intervention.
- Repeated invasive screening and surgical interventions expose patients to developing Small Bowel Syndrome which significantly decreases the chances of balloon endoscopy for small bowel polyp removal.



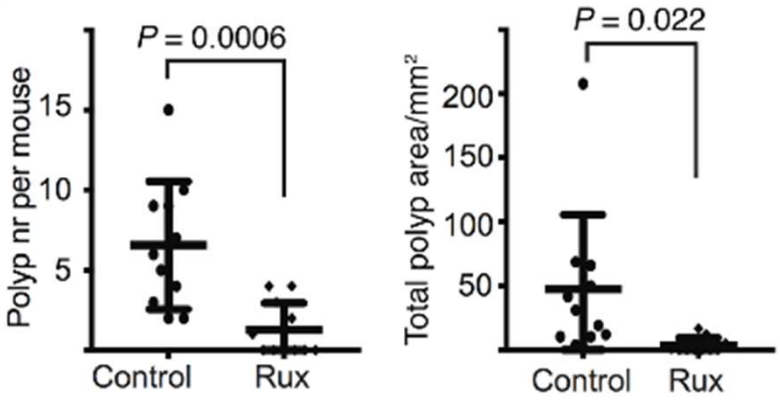
Peutz-Jeghers Syndrome

Drug Repurposing: Simple, Effective & Safe

- Jakafi (ruxolitinib) is currently approved for intermediate or high-risk mylefibrosis, including primary MF; post-polycythemia vera MF and post-essential thrombocythemia MF.
- Loss of Lkb1 in stromal cells is associated with induction of an inflammatory program including IL-11 /IL -22 production and activation of the JAK/STAT3 pathway in tumor epithelia.
- **Treatment of LKB1 deficient mice with the JAK1/2 inhibitor ruxolitinib dramatically decreased polyposis.** Ruxolitinib has therapeutic potential in PJS as evidence in the in vivo study results.

In Vivo Proof of Concept

Number and area of polyps are reduced in ruxolitinib treated *Lkb1* knockout mice.[1]



Macroscopic images of representative untreated and ruxolitinib-treated mouse stomachs.

1 J Clin Invest. 2018; 128(1):402-414. https://dio.org/10.1172/JCI93597.

Target market and opportunity

- The numbers are widely underestimated due to late diagnosis.
- Average age for cancer diagnosis in patients with PJS is 42.9 (±10.2 years). Although PJS entails a significant overall increased lifetime risk of intestinal and extraintestinal malignancy, as well as an increased risk of malignancy in younger individuals.
- Current treatment cost per screening and surgical intervention is $25k to $200k, annual or every two years, subjectively, reflective of the standard “wait and see” approach.
- There is no competitive landscape, there is no one else working on PJS treatment.
- In addition to PJS patients there is potential impact for other polyposis syndromes and cancer patients with LKB1/STK11 mutations.

Broad Therapeutic Applications

- Application for treatment in children and adults who have been diagnosed with PJS.
- Target application of where there is a more than 30% with LKB1 mutation (outside of PJS population).
- Target application with cancers of the: lung, breast, colon, stomach, small intestine, testicles, esophagus, cervix, ovaries and pancreas.
- Any cancer impacted with the LKB1 TUMOR SUPPRESSOR MUTATION, including non-small cell lung cancer where nearly half of the tumors harbor somatic and homozygous inactivating mutations in LKB1.

Competition

- No one is doing any active work on treatments for PJS.
- There is zero competition.
- This is an orphan therapeutic area. The indication is underreported, under diagnosed.
- Treatments offer board therapeutic applications.
- The intent to treat population ranges in age from toddler to adult.

Clinical Development and Regulatory Strategy

- With the results of the mouse study showing much promise, the intention is to be able to move into human trials as soon as funding is available and regulatory approval is granted.
- As this is classified as an orphan indication, and front line therapeutic, orphan drug status will be sought.
- Regulatory strategy is to first gain approval in the US, and Canada, and then in the EU (Spain, Italy, Portugal, and/or France) prior to applying for EU approval.
- FDA representative contact ready and regulatory meeting dates are to be determined.
- Ruxolitinib falls under Center for Drug Evaluation and Research (CDER) which performs an essential public health task by making sure that safe and effective drugs are available to improve the health of people in the United States.

Financials

- To-date, funding has come from a family founder that's been pursuing this for over 10 years.
- One plan is to approach the current MAH for ruxolitinib as a contributing data exchange partner.
- Immediate goal is to raise funding to commence human clinical trial phase.

Contact

Curinggenetics, Inc.
999 Corporate Drive, Suite 100
Ladera Ranch, CA 92694
info@curingenetics.org
(949) 342-6128