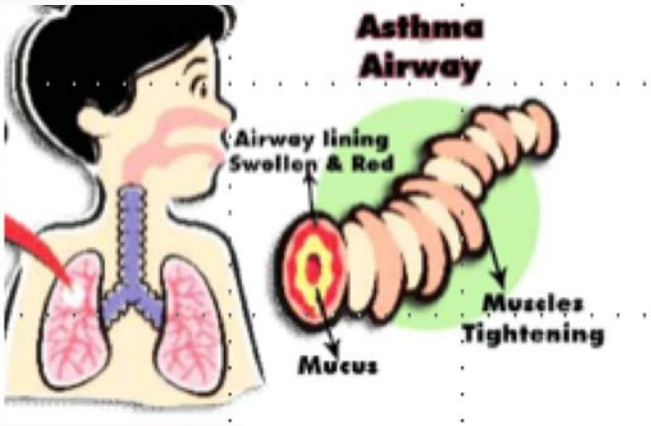
PAT-U-PAMI: Pediatric Asthma Treatment Using Painless Microneedle

► **Asthma** is the most prevalent chronic respiratory disease worldwide, **affecting more than 300 million people**. It is **the most common chronic disease in children**, affecting 8-10% worldwide.

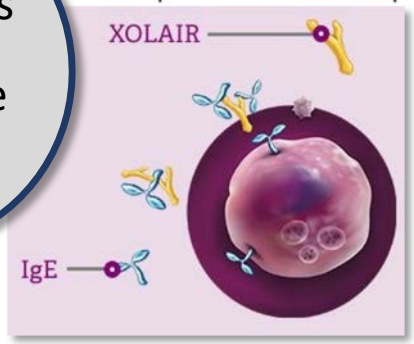
►Our **microneedle** patch eliminates the need of hypodermic needles and is relatively **painless, accurate**, and **simple** for even a parent to use for managing paediatric asthma conditions. This in turn prevent repetitive visits to clinic to inject a painful needles

What is the problem and who has it?

Affects **11%** of the children in the world



60% of the cases of severe asthma are IgE-mediated



BREAKING DOWN THE ASTHMA NUMBERS

- **7 million** U.S. children manage asthma
- **#3:** Asthma is the 3rd **leading cause of hospitalization** among children <15
- **640,000:** Annual emergency room visits for children <15
- **13.8 million:** Missed school days among children with asthma
- **$56 billion:** Yearly cost of care for a child with asthma

Source: Center for Disease Control and Prevention

5th Pediatric Allergy and Asthma Meeting (PAAM)
Bellón S et al., Clin Transl Allergy. 2018

The solution and value proposition

PRESENT: INJECTIONS OF OMALIZUMAB

- **NEEDLE-PHOBIA**
- **HUMAN ERROR**
- **INFECTION**
- **DOSAGE ERROR**

*treatment requires 1/2 injections every 2-4 weeks

* The average cost for the injected drug is $1,700 a month (doce: 150 mg, every 2 weeks)

FUTURE: MICRONEEDLE PATCHES OF OMALIZUMAB

- **PAINLESS**
- **IMPROVED IMMUNE RESPONSE**
- **MINIMAL RISK OF BLEEDING AND INFECTIONS**
- **REDUCED DRUG DOSE AND TREATMENT PERIOD**

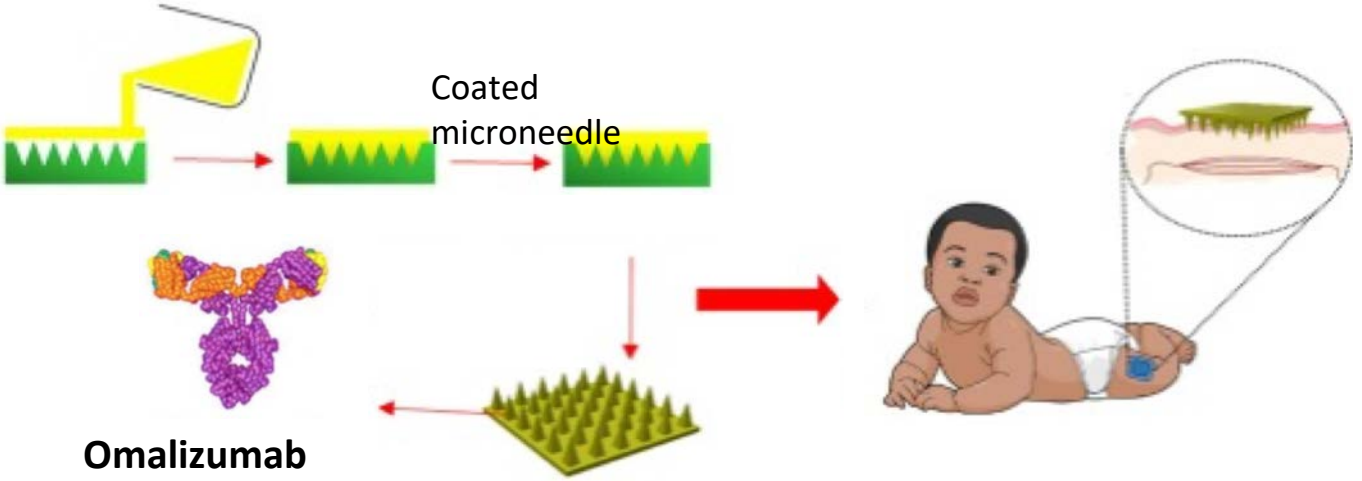
Product

Microneedles are microscopic applicators used to deliver vaccines or other drugs through transdermal application

ADVANTAGES	DISADVANTAGES
Pain free administration	Skin irritation due to allergy
Safer handling	Local inflammation
Easy to use	Can be difficult to apply
Discreetness	Tips may be broken off due to small size

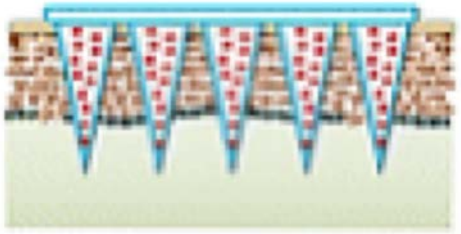
Clinical trials of microneedle-based drug delivery (54 in total)

Phase 3: Insulin
Phase 1: Lidocaine in the oral cavity
Phase 2: Adalimumab
Phase 1: Inactivated Influenza Vaccine
Phase 2b: zolmitriptan

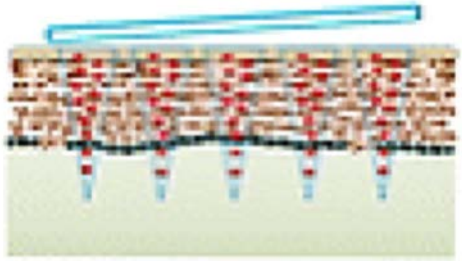


Technology

Drug-filled (omalizumab/Xolair) microneedles array using poly(vinyl alcohol)(PVA)/carboxymethylcellulose /poly(acrylic acid) (PAA) polymers



Dissolving/coated microneedle



Task 1

Design, fabrication, and characterization of microneedle mold

Task 2

Fabrication and characterization of drug-filled microneedles

Task 3

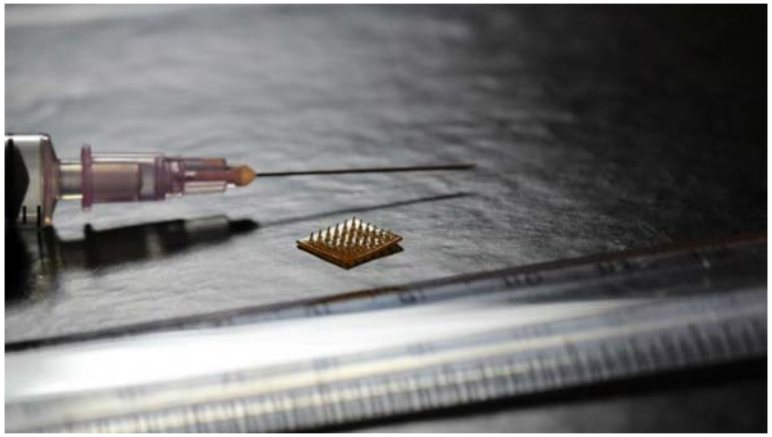
Preclinical trial in mouse model

These product can be B to C, we can sell these kind of microneedles products to clinics and pharmacies.

Comparison table with other technology

	Advantages	Disadvantages
Hypodermic needles	-Direct access to circulatory system (intravenous)	-Painful -Tissue damage -Non-autonomous administration
Needless drug delivery	-Rapid absorption (sublingual) -Economical, high dose possible (oral)	-Small dose limit - Jet may be painful
Inhalation	-Bypasses liver -Large surface of absorption	-Difficult to regulate the exact amount of dosage - Difficult to very in infants
Microneedles	-Pain free administration -**Easy to use** -Continuous and controlled release -**Safer handling** **-Self-administration**	-Local inflammation -Skin irritation

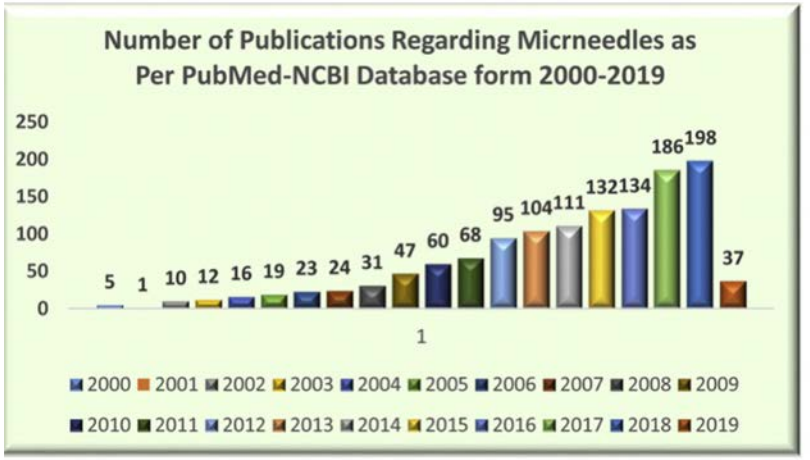
Competing approaches

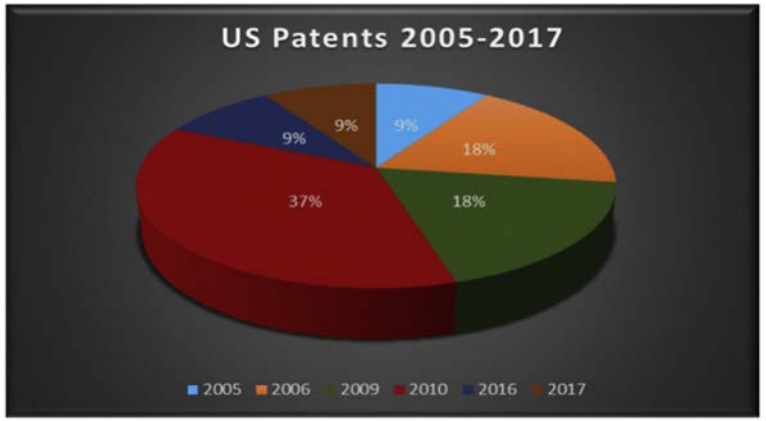


- Provides an acceptable approach to deliver the drug for parents/infants.
- Reduced needed omalizumab dosing.
- Increases the effectiveness of targeting skin resident-immune cells.
- Continuous drug delivery.
- Allows self-administration.
- Painless and safe drug administration, minimizing the risk of bleeding, infections, injuries.
- Potentially easy to produce.

Traction

1. Vinayakumar, K. B. et al. A hollow stainless steel microneedle array to deliver insulin to a diabetic rat. J Micromech and Microeng 26.6 : 065013, 2016
2. Vinayakumar, K. B., et al. "Fabrication and characterization of gold coated hollow silicon microneedle array for drug delivery." Microelectronic Engineering 128 (2014): 12-18.
3. Ferrante G, La Grutta S.The burden of pediatric asthma. Front. Pediatr. , 2018, 22;6:186.
4. Van Aalderen, W. M. Childhood Asthma: Diagnosis and Treatment. Scientifica, 2012
5. Tosca, M. A. et al. Immunotherapy and Asthma in Children. Front. Pediatr. 6, 2018
6. Normansell R. et al. Omalizumab for asthma in adults and children. Cochrane Database Syst Rev. (1): CD003559, 2014
7. Sanjukta D. et al. Recent Advances in Microneedle-Based Drug Delivery: Special Emphasis on its Use in Paediatric Population. Eur J Pharm Biopharm, 2019





We look for the new collaborations and grants related to H2020 or US-Europe collaborated research fundings to extend the project.

Team

Team Members

Vinaya Kumar K B

- Staff researcher.
- International Iberian Nanotechnology Laboratory (INL), Portugal.
- Experience in the development of several Microelectromechanical systems (MEMS) devices.

Verónica Miguel

- Postdoctoral researcher.
- Center of Molecular Biology in Madrid (Spain).
- Molecular and cell biology techniques applied to the generation of *in vivo* mouse models.

Mentor

Wolfgang Krull

- Senior Management Professional in the Medical Device Industry.
- Experience includes high-tech medical devices, hardware, software, x-ray, 2D/3D imaging, patient monitoring, quality systems, ISO 13485 and FDA

Closing slide

► Microneedle-based omalizumab delivery is a safer promising strategy for the treatment of infant asthma.

► The effect of drug dissolution/effectiveness in skin layers (microneedle-based delivery) is the same compared to hypodermic needle-based delivery.

► Acceptance among the doctors and patients for microneedle based-omalizumab delivery.

Prausnitz MR et al., Curr Top Microbiol Immunol. 2009

Update for IDEA2

1. Prepared questionnaire for the doctors and parents
2. Checked the FDA approval criteria for the Microneedle technology*
3. Spoke to 2 pediatric doctors in portugal
    a. Doctor showed an interest in our product but they are little concerned about the cost.

*https://www.fda.gov/media/107708/download