



# Sublingual Vaccination by an Oro-Dispersible Patch made with Natural Polymers :: Optimization for Vaginal and Rectal Protection

Anne-Lise Paris, Evelyne Colomb, Mélanie Bellina, Bernard Verrier, Claire Monge

## ► To cite this version:

Anne-Lise Paris, Evelyne Colomb, Mélanie Bellina, Bernard Verrier, Claire Monge. Sublingual Vaccination by an Oro-Dispersible Patch made with Natural Polymers :: Optimization for Vaginal and Rectal Protection. Mucosal Immunology Course and Symposium, Jul 2020, Denver, United States. hal-03758939

**HAL Id: hal-03758939**

**<https://hal.science/hal-03758939>**

Submitted on 1 Sep 2022

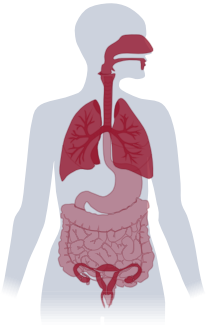
**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Sublingual Vaccination by an Oro-Dispersible Patch made with Natural Polymers: Optimization for Vaginal and Rectal Protection

AL. Paris<sup>1</sup>, E. Colomb<sup>1</sup>, M. Bellina<sup>1</sup>, B. Verrier<sup>1</sup>, C. Monge<sup>1</sup>

<sup>1</sup> Laboratoire de Biologie Tissulaire et d'Ingénierie Thérapeutique, (LBTI) UMR 5305, Université Lyon 1, CNRS, IBCP, Lyon, France

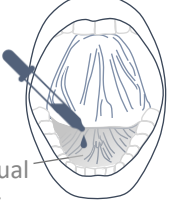


### Context

Mucosae represent preferential entry sites for pathogens. Consequently, the mucosal immune system has been shaped to act as the **first line of defense** to prevent microorganisms' invasions. By **sublingual vaccines** administration, protection can be achieved with **both systemic and local immune response** induction, as well as **rectal and vaginal protection**.

### Sublingual liquid vaccines:


Heterogeneity due to partial dilution in saliva



Sublingual Floor  
Floor of the mouth: 10 – 100  $\mu$ m

### Introduction

#### Oro-dispersible membrane:

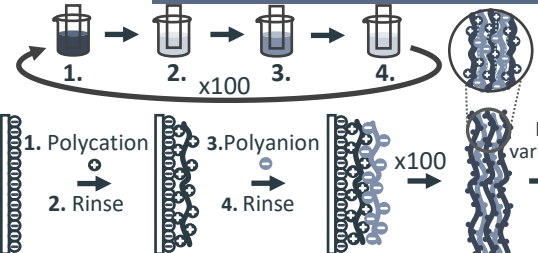


Bioactive vaccination patch containing subunit antigens and protein or nanoparticulate adjuvants

### Sublingual vaccination patch

- Biocompatible**  
Composed with polysaccharides which are not toxic for cells and mucosae
- Functionalizable & Biodegradable**  
Protein antigen & adjuvant incorporation without bioactivity loss. Antigen released during patch degradation by salivary enzymes.
- Mucoadhesive**  
Lengthen contact time between formulation and mucosa to induce a better response
- Bioactive**  
Induce a systemic and mucosal immune response

### Layer-by-Layer technique



1. Polycation 2. Rinse 3. Polyanion 4. Rinse

x100

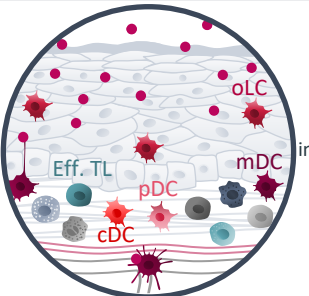
pH variation

protein & NP

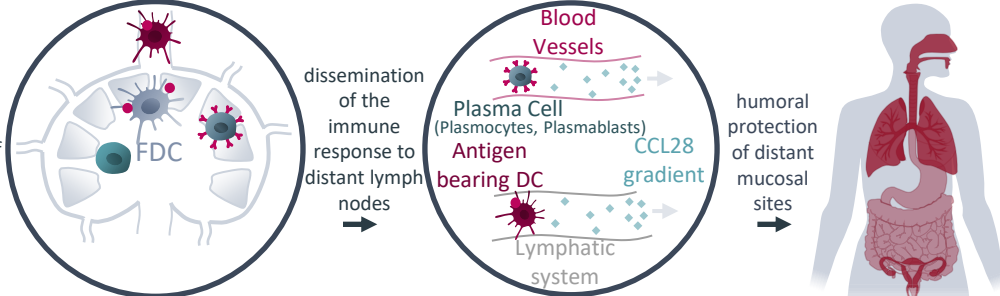
pH variation

sublingual delivery

### Strategy



initiation of adaptive response



dissemination of the immune response to distant lymph nodes

humoral protection of distant mucosal sites

Blood Vessels

Plasma Cell (Plasmocytes, Plasmablasts)

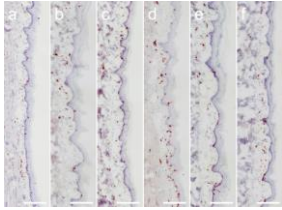
Antigen bearing DC

CCL28 gradient

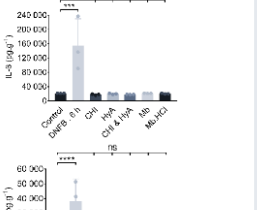
Lymphatic system

### Biocompatible

MHC-II IHC at sublingual site after patch adm.



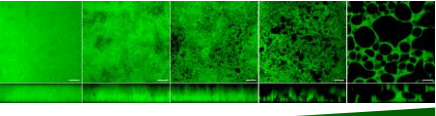
Cytokines quantification after patch adm.



### Biodegradable & functionalizable

Fluorescent patch (in green) degradation in salivary enzymes

30 minutes 3 heures 6 heures 24

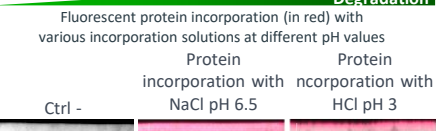


Degradation

Fluorescent protein incorporation (in red) with various incorporation solutions at different pH values

Protein incorporation with NaCl pH 6.5

Protein incorporation with HCl pH 3

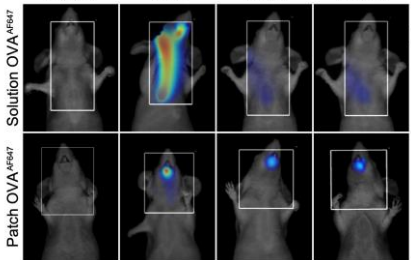


### Results

#### Mucoadhesive

Fluorescent protein delivery *in vivo* with patch or as solution

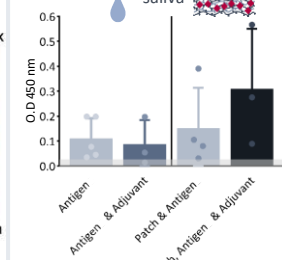
Control 2 min 10 min 30 min



#### Bioactive

Specific antibodies after patch adm. *In vivo*

Specific IgA antibodies in saliva



### Conclusion & Perspectives

Our results demonstrate this oro-dispersible patch biocompatibility through IHC and cytokines quantification after patch administration. This patch permits protein incorporation using various pH, allowing protein release once degraded by salivary enzymes. Its mucoadhesive properties permits a prolonged delivery at the sublingual site inducing a higher quantity of specific IgA in saliva. For an enhanced mucosal response, especially at distant mucosal sites (such as rectal and vaginal mucosa), other mucosal adjuvants should be tested, especially through NP formulation for a better presentation to immune cells.