

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

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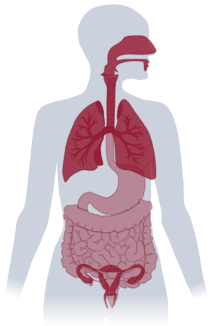
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Sublingual Vaccination by an Oro-Dispersible Patch made with Natural Polymers: Optimization for Vaginal and Rectal Protection

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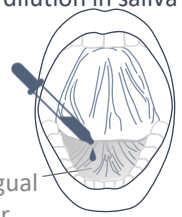
Introduction



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



Floor of the mouth: 10 – 100 µm

Oro-dispersible membrane:



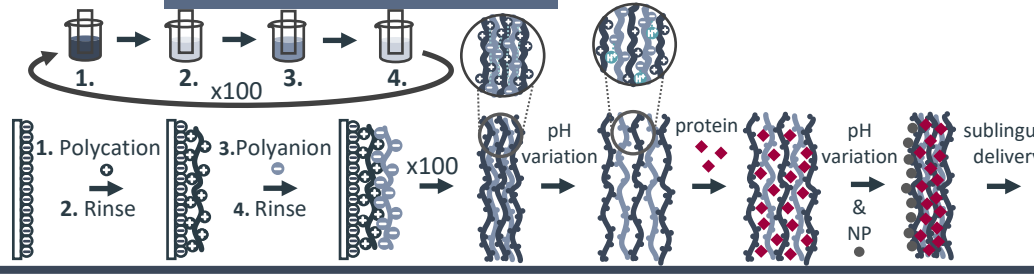
Bioactive vaccination patch containing subunit antigens and protein or nanoparticular adjuvants



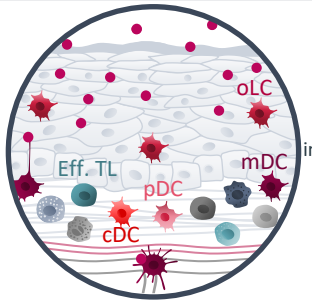
Sublingual vaccination patch

- **Biocompatible**
  Composed with polysaccharides which are not toxic for cells and mucosae
- **Functionalizable & Biodegradable**
  Protein antigen & adjuvant incorporation without bioactivity loss. Antigen relased 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

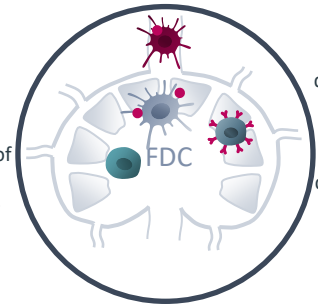
Layer-by-Layer technique



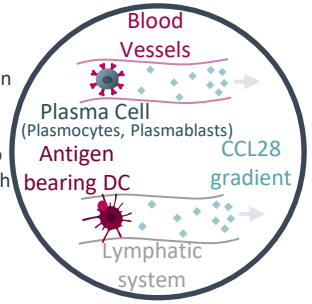
Strategy



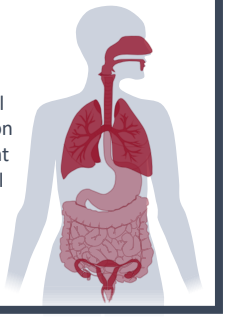
initiation of adaptive response



dissemination of the immune response to distant lymph nodes



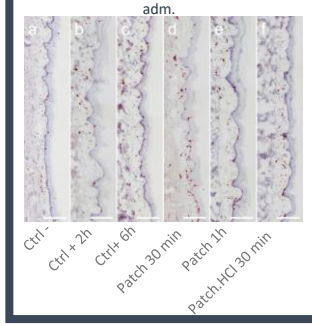
humoral protection of distant mucosal sites



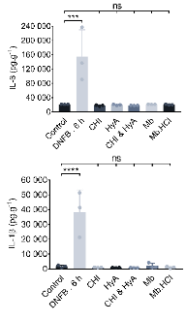
Results

Biocompatible

MHC-II IHC at sublingual site after patch adm.

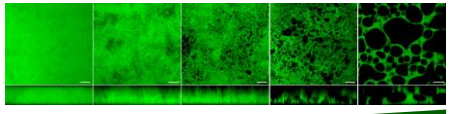


Cytokines quantification after patch adm.



Biodegradable & functionalizable

Fluorescent patch (in green) degradation in salivary enzymes



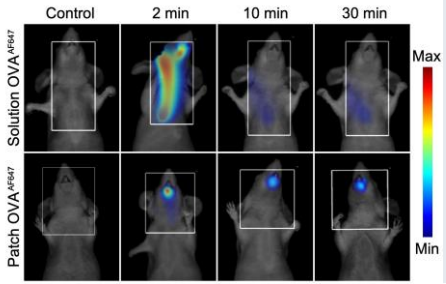
Dégradation

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



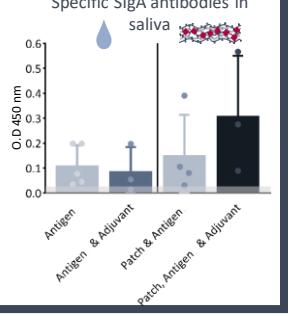
Mucoadhesive

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



Bioactive

Specific antibodies after patch adm. *In vivo*



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 sIgA 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.