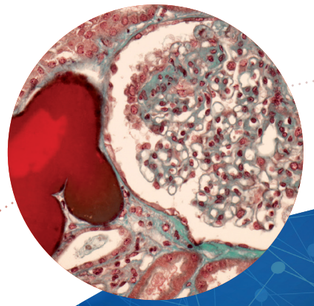
→ THERAPEUTIC VACCINES

Antiretroviral therapy does not cure HIV infectionnordoesitallowrestorationand/or development of virus-specific immune responses capable of controlling HIV replication. Therapeutic vaccination and immune interventions that generate new or boost pre-existing HIV-specific T-cell responses are being investigated as a potential means to achieve a functional HIV cure. Previous studies have shown modest efficacy in suppressing virus replication in experimental animal models and in patients despite increasing HIV-specific immune responses. It is generally thought that the profile of HIV-specific immunity induced by these immunisation strategies is suboptimal in terms of breadth, magnitude and functional profile of the induced T-cell responses. These observations indicate that better vaccines, improved immunization strategies, combined with reservoir mobilizer and immunomodulators must be explored in the development of functional cure strategy.

Building on the advances in HIV vaccine research and addressing key limitations to vaccine efficacy, **EHVA aims to build a robust discovery and clinical research platform for novel therapeutic and prophylactic vaccine candidates,** with the aim to generate more durable and potent immune responses. At the same time, the programme will develop **new tools to help identify the correlates of immunity, optimize vaccine regimens and aid the selection of novel vaccine candidates** for further development.



HIV-Associated Nephropathy

Consortium and Partners

To achieve its goal, **EHVA** has brought together the expertise in the fields of molecular biology, structure biology, vectorology, adjuvants delivery, immunology, clinical science, biostastitics, virology manufacturing, and industrial development. The partners of **EHVA** are leading scientists in their correspondent field with proven publication track records and international recognition of their leadership within the scientific community, working in close collaboration with representatives of the HIV community. **EHVA** brings together the complementary skills and expertise of 39 groups with an integrated approach to tackle the scientific challenges.

- *Institut national de la santé et de la recherche médicale* **INSERM** FR *(Y. Levy, JD. Lelièvre, R. Thiébaut)*
- *Hospices Cantonaux* **CHUV** SZ *(G. Pantaleo)*
- *Sanofi Pasteur* **SA** FR *(S. Phogat)*
- *Consorci Institut d'Investigacions Biomèdiques August Pi i Sunyer* **IDIBAPS** ES *(F. Garcia)*
- *Heinrich-Pette Institut Leibniz Institut Fuer Experimentelle Virologie* **HPI** GE *(M. Altfeld)*
- *Imperial College of Science, Technology and Medicine* **IMPERIAL** UK *(J. Weber)*
- *Istituto Superiore di Sanità* **ISS** IT *(S. Vella)*
- *Universitaet Regensburg* **UREG** GE *(R. Wagner)*
- *Karolinska Institutet* **KI** SE *(P. Liljeström)*
- *Universitaet Zuerich* **UZH** SZ *(A. Trkola)*
- *Fondazione per l'Istituto di Ricerca in Biomedicina* **IRB** SZ *(A. Lanzavecchia)*
- *Universitaetsklinikum Hamburg-Eppendorf* **UKE** GE *(J. Schulze zur Wiesch)*
- *The Chancellor, Masters and Scholars Of The University Of Oxford* **UOXF** UK *(Q. Sattentau)*
- *Universite Grenoble Alpes* **UGA** FR *(W. Weissenhorn)*
- *Academisch Medisch Centrum bij de Universiteit van Amsterdam* **AMC** NL *(G. de Bree)*
- *Stichting Biomedical Primate Research Center* **BPRC** NL *(W. Bogers)*
- *Ludwig-Maximilians-Universitaet Muenchen* **LUM** GE *(M. Hoelscher)*
- *Medizinische Universität Innsbruck* **MUI** AT *(D. Holm-von Laer)*
- *Agencia Estatal Consejo Superior De Investigaciones Cientificas* **CSIC** ES *(M. Esteban)*
- *Université de Lausanne* **UNIL** SZ *(M. Lawrenz)*
- *Erasmus Medical Center* **Erasmus** NL *(C. Boucher)*
- *Stichting International AIDS Vaccine Initiative* **IAVI** NL *(H. Kuipers)*
- *FIT Biotech Oy* **FIT** FI *(K. Reijonen)*
- *EuroVacc Foundation* **EuroVacc** SZ *(S. Ding)*
- *Fred Hutchinson Cancer Research Center Non Profit Corporation* **FHCRC** US *(R. Gottardo)*
- *Commissariat A L'Energie Atomique Et Aux Energies Alternatives* **CEA IDMIT** FR *(R. Le Grand)*
- *Universitaet Bern* **Unibe** SZ *(M. Bachman)*
- *Janssen Vaccines & Prevention B.V* **Janssen** NL *(H. Langedijk)*
- *Uganda Virus Research Institute* **UVRI** UG *(P. Kaleebu)*
- *National Institute for Medical Research - Mbeya Medical Research Centre* **NIMR** TZ *(L. Maboko)*
- *Instituto Nacional de Saude* **INS** MZ *(I. Jani)*
- **PAC-CI** IV *(T. Yoman)*
- *University College London* **UCL** UK *(S. McCormack)*
- *The University of Liverpool* **ULIV** UK *(W. Paxton)*
- *The General Hospital Corporation* **GHC** US *(G. Alter)*
- *Vrije Universiteit Brussel* **VUB** BE *(K. Thielemans)*
- *Istituto Nazionale Malattie Infettive L.Spallanzani - IRCCS* **INMI** IT *(G. Ippolito)*
- *European AIDS Treatment Group* **EATG** BE *(G. Corbelli)*
- *Inserm Transfert* **IT** FR *(S. Rémola)*
- *International AIDS Vaccine Initiative* **IAVI Inc** US *(J. Gilmour)*

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Context

Despite enormous progress in the prevention and treatment for HIV and AIDS, the global response cannot keep pace: almost **37 million people are living with HIV worldwide with around 6,000 new HIV infections each day.** Whilst the vast majority of new infections occur in Sub-Saharan Africa, the past year has also seen over 142,000 new infections in the European region. HIV vaccine is essential to cut new HIV infections, ensure a sustainable response to HIV/AIDS, save the lives of millions of people and ultimately help achieve an end to the epidemic.

Infected macrophages by HIV

→ PREVENTIVE VACCINES

In the more than 30 years of HIV vaccine research, a variety of vaccine approaches including those generating antibodies and activating T-cells have been developed and evaluated. One of these candidates showed an ability to partially reduce the risk of HIV infection – but insufficient to justify plans for roll-out. In a new efficacy trial, recently initiated in South Africa, researchers will test an adapted vaccine regimen in order to improve on these results. In addition, more than 20 HIV vaccine candidates are in early clinical development, and innovative approaches are being evaluated in preclinical settings. Whilst these could generate new promising vaccine candidates, in the absence of correlates of protection and a proven selection platform, researchers are facing difficult choices on how to select the best candidates and immunization strategies, including but not limited to the different prime-boost combinations, number of injections and injection intervals. There is an urgent need to develop tools to help identify the correlates of immunity, optimize vaccine regimens and aid the selection of novel vaccine candidates for further development.

Objectives & strategy

Fostering a multidisciplinary approach to HIV vaccine development

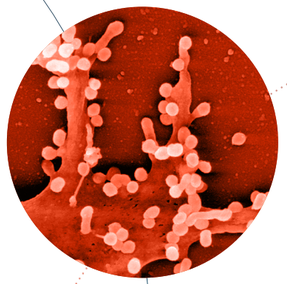
The European HIV Vaccine Alliance (**EHVA**) programme aims to develop a **Multi-disciplinary Vaccine Platform (MVP)** for prophylactic and therapeutic HIV vaccines through four major approaches.

1. Discovery Platform, to generate novel prophylactic and therapeutic vaccine candidates that can induce potent neutralising and non-neutralising antibody responses and T-cell responses. Specifically, improving HIV envelope protein-based vaccine immunogenicity and vaccine regimens and achieving the transient break of immunological tolerance.

2. Immune Profiling Platform, to rank novel and existing (benchmark) vaccine candidates in pre-clinical and human clinical trials; the ranking will be performed through the use of a large set of validated, qualified and standardised immunological assays and access to the most advanced technologies in the profiling of the immune responses.

3. Data Management and Down-Selection Platform, to provide powerful statistical tools for the analysis and interpretation of complex data and algorithms for the efficient selection of vaccine candidates at the different stages, i.e. pre-clinical and clinical, of vaccine development.

4. Clinical Trials Platform, to accelerate the clinical development of novel vaccine candidates and the early prediction of failure of vaccine candidates. This will be achieved through innovative trial designs such as Experimental Medicine (EM) Trials and Adaptive Design, aimed at identifying improved vaccine regimens in the prophylactic setting and of immune correlates of protection in the therapeutic setting.



Viral Particle of HIV

Hypothesis

On the basis of the **Objectives** outlined above, the following hypotheses will be tested:

1. The increase in the immunogenicity of novel Env protein-based vaccine candidates together with the selection of optimal prime/boost combinations and transient break of immunological tolerance will result in the induction of improved quantitatively and qualitatively antibody responses as compared to benchmark vaccine regimens.

2. The immune profiling using an algorithm of **EHVA** immunological assays will provide the delineation of the diversity of the immune response induced by different vaccine candidates and the identification of immune correlates of protection.

3. The down-selection criteria for the novel vaccine candidates will allow efficient progression of the best-in-class vaccine candidates from the pre-clinical to the clinical development and early prediction of vaccine failure.

4. The innovation in clinical design will allow the elimination of poorly immunogenic vaccine candidates at early stages of clinical development and accelerate the progression of the best-in-class vaccine candidates into larger clinical trials.

Expected Outcomes

EHVA will contribute to achieving safe and effective prophylactic and therapeutic vaccines to combat HIV/AIDS, notably by enhancing the identification and accelerating the development of promising vaccine candidates. The programme will develop novel vaccine concepts and a robust screening platform for vaccine candidate selection, supported by appropriate clinical trial design and infrastructure, capabilities for broad immunological profiling, standardized assays and data management and integration. The expertise, knowledge and resources that **EHVA** aims to develop will provide an indispensable resource for the HIV vaccine research community, and can help to achieve:

- Reduced R&D cost through improved methods for selecting best-in-class vaccine candidates in early stage research, increasing the number of candidates that can be evaluated with limited resources, thus increasing the chance of achieving effective vaccines
- Increased capacity and resources for the further clinical development of promising vaccine candidates in regions where vaccines are most needed, including through the relationship with the European and Developing Countries Clinical Trial Partnership (EDCTP)
- Improved innovation capacity and the integration of new knowledge, notably through close collaboration with the industrial partners for product development