

AIDS and Immunosuppression Program

The National Institute of Dental and Craniofacial Research (NIDCR), National Institutes of Health (NIH), is the primary sponsor of oral, dental and craniofacial biomedical and behavioral research and research training in the United States. Through the AIDS and Immunosuppression Program in the Integrative Biology and Infectious Diseases Branch, the Institute supports extramural basic, translational and clinical research on HIV infection and AIDS to advance understanding of the underlying molecular, cellular, immunological and genetic mechanisms that enable or prevent HIV infection and development of oral complications and malignancies (oral cancers) associated with AIDS. In addition, this program encourages research that is responsive to the NIH Common Fund Initiatives.

Pathogenesis & Immunopathogenesis Research: Molecular and Immunological Mechanisms of Oral Manifestations of HIV/AIDS, Oral Opportunistic Infections and Oral Malignancies in Immunosuppressed Individuals

NIDCR funds research to develop biomedical and behavioral strategies to prevent oral transmission of HIV as well as oral manifestations and oral malignancies (cancer in the oral cavity) associated with HIV infection and AIDS. Oral infections associated with immunosuppression have been described as initial manifestations of HIV infection and are markers for disease progression. NIDCR supports research on the pathogenesis of HIV-related oral complications and cancers due to infections from HIV and oral opportunistic viruses, bacteria and fungi. NIDCR also supports molecular, cellular, immunological and genetic mechanisms that facilitate the development of HIV-related oral diseases, and approaches to prevent these diseases, interactions between HIV and oral pathogens, characterization of the oral microbiome, virome, and fungizome in the context of HIV/AIDS, mechanisms of viral-induced and AIDS-related oncogenicity (oral cancers), and the use of system biology approaches to understand the immunopathogenesis of, and the therapeutic and prophylactic treatments against AIDS related oral manifestations and malignancies. Priority research areas also include studying the pathogenesis, prevalence and severity of oropharyngeal lesions or malignancies caused by oral pathogens such as Epstein Barr virus (EBV), cytomegalovirus (CMV), herpes simplex virus (HSV), human papillomavirus (HPV), Kaposi's sarcoma associated virus (HHV8), polyomavirus, and bacterial and fungal species.

Oral HIV Transmission/Inflammation/Pain/AIDS-related Oral Pathogens

NIDCR supports research to better understand oral HIV transmission, emergence of HIV variants, oral HIV infection and

co-infections by AIDS-related oral pathogens to develop safe and effective prophylactic and preventive strategies to block HIV and oral pathogen infections. In this regard, the role of the oral mucosal and innate immune systems connected with induced adaptive and systemic immunity is an important area of study. Similarly, understanding early and subsequent events of HIV transmission and infection through the oral route, development of inflammation and pain, and co-infection by oral pathogens remain important areas of study. Studies have shown that HIV infection can occur via the oral route with exacerbated prevalence of oral pathogen infections. Acquisition of HIV and oral pathogens through the oral mucosa (e.g., HIV exposure through oral sex or breast milk) and developing oral prophylactic and prevention strategies against HIV and oral pathogens are research priorities. The NIDCR equally supports studies that examine the immunology, structure, biology, host genetics, physiology and biochemistry of the oral mucosa regarding susceptibility or resistance to HIV infection and replication as well as infection by AIDS-related oral pathogens.

Oral Mucosal Immunity/Clinical Research/ Oral Mucosal Vaccines against HIV and Oral Viruses

An intact immune system is necessary for good oral health. For that reason, NIDCR supports basic, translational, and clinical research on developing oral prevention strategies against HIV and oral pathogen infections in healthy individuals. Similarly, NIDCR supports the development of novel therapeutic strategies for subjects with HIV/AIDS who have co-infections with oral pathogens and develop oral lesions and malignancies. Research on immune enhancement through the use of oral prophylactic vaccines, oral immunotherapies, oral topical formulations, or biological modifiers is central to designing effective and safe methods to block and/or to treat HIV infection, AIDS-related oral complications and AIDS-associated malignancies. NIDCR supports research on oral

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mucosal prophylactic vaccines against HIV and oral viruses that use the oral route and tissues for delivery to boost local (i.e., oral innate and mucosal immunity) and systemic innate as well as adaptive immunity. Similarly, NIDCR funds non-interventional and interventional clinical research studies in children, adolescents and adults to develop a comprehensive approach to improve the clinical diagnosis, treatment, and management of co-morbidities and malignancies of AIDS-related oral complications. The NIDCR-sponsored clinical studies are conducted through: 1) the Oral HIV/AIDS Research Alliance (OHARA, <https://actgnetwork.org/OHARA>) a Collaborative Science Group of the AIDS Clinical Trials Group (ACTG) in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID); and 2) the Pediatric HIV/AIDS Cohort Study (PHACS, <https://phacs.nichdclinicalstudies.org/default.asp>) in collaboration with the National Institute of Child Health and Human Development (NICHD).

Diagnosis/Prevention and Therapeutic Research/ Integrative Biology

The NIDCR supports research on early detection, prevention, and treatment of HIV infection, AIDS, oral pathogens associated with HIV/AIDS, and oral malignancies related to HIV/AIDS. The identification of molecular, immunological, and cellular basis to inhibit AIDS-related polymicrobial organisms (e.g., bacteria species, *Candida* and other fungi, EBV, HPV, CMV, HSV, HHV8, polyomavirus, and HIV infection) by factors expressed in saliva and oral mucosal tissues is a NIDCR research priority. Studies focused on determining the mechanisms of action of oral factors against oral pathogens and modeling biologically active peptide regions within the pathogens are supported by NIDCR. Research to construct bioactive synthetic peptides and recombinant salivary proteins, and to develop systems for their delivery is encouraged. Integrative diagnostic, preventive and therapeutic approaches connecting oral health status in HIV/AIDS individuals with systemic disease (e.g., metabolic, nutritional, endocrine, cardiovascular, renal, bone, skeletal muscle, central nervous system, and skin disease complications associated with HIV infection and treatment) are also encouraged. Oral specimen based diagnostics for HIV, other oral viruses, bacteria and fungi in novel assays, with new technologies and with different field applications (e.g., point of care assays and rapid tests) is a research priority.

SPECIFIC AREAS OF INTEREST

- ✓ Etiology, Transmission, Pathogenesis, Immunopathogenesis, Prevention and Therapeutics Research linked to HIV, Oral Opportunistic Infections and Complications caused by Viruses, Bacteria and Fungi
- ✓ Immunotherapies & Oral Topical Formulations
- ✓ HIV/AIDS Oral Immunology & Oral Prophylactic Vaccines Against HIV and Other Oral Viruses
- ✓ HIV/AIDS Biomarkers & Oral Specimen Based Diagnostics
- ✓ Cellular Reprogramming by Oral Viruses, Genetic Variation, Epigenomic Changes of Oral Viruses, and Glycomics
- ✓ AIDS-Related Oral Cancers, Diagnostics, Prevention and Therapeutics
- ✓ *Candida* & fungal/biofilm interactions and Infections
- ✓ Non AIDS-Related Immunosuppression (Effects on Infection)

Future Directions

Areas of specific need: molecular and cellular mucosal immunobiology, virology, genomics, proteomics, glycomics, epigenomics, metabolomics, and systems biology; development of improved animal and *in vitro* models; biomarkers to detect host component changes due to oral infectious diseases; functional, high throughput, incidence and high potency assays for oral pathogen detection, screening and diagnosis; oral prophylactic vaccines against HIV and other viruses causing oral lesions and diseases; novel immunotherapies and therapeutic interventions for oral infectious diseases; viral immunology and immunopathogenesis research that will enhance the ability to study oral innate, oral mucosal and adaptive immune function in oral mucosal tissues; enhancement of innate and adaptive oral immune response to HIV and other oral infections and malignancies (e.g., HPV-induced oral cancers) associated with immunocompromised conditions.

Additional Information

For further information about the NIDCR AIDS and Immunosuppression Program, please contact:

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Funding Opportunity Announcements (FOAs)

PA-10-290: Research on Malignancies in the Context of HIV/AIDS (R01)
<http://grants.nih.gov/grants/guide/pa-files/PA-10-290.html>

PA-10-291: Research on Malignancies in the Context of HIV/AIDS (R21)
<http://grants.nih.gov/grants/guide/pa-files/PA-10-291.html>

PA-11-333: Immunopathogenesis of HIV/AIDS-related Oral Manifestations and Host Immunity (R21)
<http://grants.nih.gov/grants/guide/pa-files/PA-11-333.html>

PA-11-334: Immunopathogenesis of HIV/AIDS-related Oral Manifestations and Host Immunity (R01)
<http://grants.nih.gov/grants/guide/pa-files/PA-11-334.html>

Note: Unsolicited R01 applications are welcome.