

## **Competence Network for HIV/AIDS - Description of the scientific foci**

The Scientific Committee in collaboration with the Scientific Boards and the CO defined five scientific topics as the main focus of further research within the CompNet: ageing, oncological diseases in the course of HIV/AIDS, psychosocial and neurological impairments, biomedical research and prevention and research on children and pregnancy.

These subjects were chosen because they facilitate innovative research on an international significant level. Additionally, the item structure of the patient cohort provides a very good basis as to research on these topics. Partly, the projects are dependent on each other, so, and additional scientific benefit due to synergy effects between research projects within these foci will be achieved. Prospective as well as retrospective projects with direct links to the patient cohort of the CompNet are envisaged. In terms of prospective studies, retrospective data of the patient cohort will always be used to enlarge the potential data basis for analyses.

The five scientific foci are defined as follows.

- Biomedical research and prevention
- Ageing
- Oncological diseases in the course of HIV/AIDS
- Psychosocial and neurological impairments due to HIV/AIDS
- Research on children and pregnancy

### **Biomedical research and prevention**

Of special importance within the CompNet HIV/AIDS is the recognition and use of patient data and patient derived materials for basic and patient oriented research that leads to new, biomedicine based approaches in prevention. In the previous funding period, immunological methods have been standardised and proven to be an asset for the ongoing clinical vaccine trials. A broader scope is however necessary to cover the needs of personalized medication and insights into vaccine induced correlates of protection from infection and/or from development of clinical AIDS on a molecular level. Two important and powerful technologies are based on DNA-arrays. Whereas pharmacogenomic approaches trace differences in the reactions of different individuals to the same drug back to genetic differences in the recipients, expression profiling concentrates on differences in the host response, driven by variant pathogens or vaccine formulations.

Pharmacogenomics attempt on the level of analysing the host genome to find explanations correlations of clinical symptoms, effects and undesirable side-effects of various pharmaceutical products with individual genotype differences. It is the goal to administer medications in formulations optimized for the respective patient, to optimize effectiveness and reduce or eliminate negative side effects. It is expected that the cohort will be a rich source for such studies.

Chip-based technologies for expression profiling governed by bioinformatics can be used to analyse the host response to an infectious agent in a broad view. This allows to study novel aspects such as a wide scope on innate immunity, as well as other cellular signal exchanges into the assessment of control of pathologic consequences of viral and other infections. Starting these platforms will be greatly facilitated by having elite controllers, rapid progressors and

patients with average course of the HIV infection available for initial work on expression profiling and well documented patient-groups with severe side-effects of therapy such as lipodystrophy for an analysis of genetically fixed cofactors.

Analyses of influencing factors on the clinical course of HIV-infection are an additional approach to improve prevention based on a biomedical level. On the one hand side, a better knowledge of these factors can allow to shape more appropriate therapies on an individual level to strengthen compliance to HAART and improve prevention on a secondary level. On the other hand side, a more effective therapy means better clinical outcomes (e.g. lower viral loads) and is, therewith, an important factor to reduce the risk of HIV-transmission. Considering all that, the CompNet plans to establish clinical studies which will be automatically linked to basic science to clarify the mechanisms underlying clinical observations.

People who are living with HIV or an AIDS-related disease are crucial in ensuring the success of prevention interventions and must be targeted accordingly, including voluntary HIV testing and counseling. The cohort of the CompNet HIV/AIDS offers an unique opportunity to conduct socioscientific analyses with regard to biomedical HIV prevention (e.g. through HAART, PEP, PREP, microbicides or circumcision).

## **Ageing**

Since the introduction of highly active antiretroviral therapy (HAART) in 1996, HIV infection has become a chronic disease. Due to patients' longer survival times, cofactors and co-morbidities, such as physiological ageing, vascular risk factors, neuro-cognitive deficits, cancer, Hepatitis C co-infection and psychiatric diseases, influence the course of the infection "on the long run".

Thus, clinical studies will clarify the interactions of co-factors and co-morbidities of HIV-disease with antiretroviral therapy and will be the basis to explore therapeutic strategies for a control of these co-factors. For example, neuro-cognitive deficits do not respond in every case positively to HAART; due to that, additional therapies have to be established to prevent patients from getting severely impaired or develop HIV-associated dementia "triggered" by e. g. normal ageing. As a basis for that, the epidemiology of HIV in older populations will be described, analysing the high share of older persons within the patient cohort (1,749 persons  $\geq$  50 years, thereof 598 persons  $\geq$  60 years).

Ageing is also a determining aspect for several important sociological parameters in the field of HIV infection. With an increase in age, the perception and the attitude to HAART may change and will result in major consequences for the adherence to therapy. However, HIV infection can impair the body perception and by that accelerate the subjective perception of ageing. Here, cross-links exist to the clinical science board, where this topic will be investigated under a clinical and medical-somatic point of view. Concerning this topic, different levels of perception and perspectives have to be distinguished: amongst others, a subjective- vs. a HIV specific- vs. a clinical view (e.g. described by surrogate markers). Thus, cross-links in the topic of ageing relay also to the Scientific Board Gender and Pediatric Sciences regarding gender specific aspects, partnership, sexuality and the important area of social and sexual networks.

## **Oncological diseases in the course of HIV/AIDS**

Oncological diseases such as Kaposi sarcoma were of great importance regarding the later stages of HIV-infection as AIDS-associated tumours, but their incidence decreased during the last years. However, there is a recent distinct increase of impact in HIV-infected persons from tumors which are currently not defined as AIDS-associated. There is evidence that the incidence and prevalence of HPV-associated tumours increased in HIV-infected persons in the last

years, but a correlation to HIV infection is not sufficiently proven by now. In this context, particularly HPV-related anal carcinoma and genital dysplasia are of high importance. Additionally, it is assumed that HPV could increase the risk of acquiring a HIV-infection distinct.

As a consequence, one of the scientific foci of the CompNet is to survey incidences and prevalences of oncological diseases, in particular also the epidemiology of lung cancer and lymphomas as well as to clarify underlying mechanisms for the exclusion of these specific tumours from the overall benefit of HAART. Therefore, research on the course and effects of HAART and supplementary therapies will be a third focus.

### **Psychosocial and neurological impairments due to HIV/AIDS**

HIV infection can have a manifold psychosocial and neurological impact on those affected, due to the transmission risks and the way that HIV infection progresses. Additionally, psychosocial factors are often present prior to HIV infection and influence the infection and its development in multiple ways and have also a big impact on individual preventative behaviour. Both psychosocial and neurological impairments can have important consequences for coping with the disease; primary prevention of infection; planning for the individual future, eg. in terms of work life; issues of partnership, profession and career; potential barriers to obtain adequate support, located in patients as well as in professionals; cultural specificities, e.g. in migrants (1,521 person given in the new cohort), who may be particularly affected by HIV. In addition, numerous implications for health-economics result from both the point of view of people living with HIV and AIDS (PLWHA) and from that of payers and providers of medical care. Important and specific national characteristics in this field are consequences of the particularities of the German health care system and its shared funding by public and private health insurances as well as the comparatively low HIV incidence and prevalence in Germany since decades.

Results of research on these topics should be able to describe or to uncover specific conditions and mechanisms particularly in the field of HIV infection. The envisaged research projects can help in a result-oriented manner to find rational based societal decisions and to optimise allocations in the public health system.

In the past, the emphasis of social science research in Germany had not been oriented towards research with larger cohorts. Although a backlog must be stated for basal and descriptive research, special opportunities arise through the availability of the database of the German CompNet cohort on HIV/AIDS for social research. The CompNet database will allow to accomplish unique and fundamental analyses as to the specific German situation, in combination with supplemental questionnaires to be used occasionally.

Combining competences given in the relevant Scientific Boards, research within CompNet will focus on these topics and on the specific linkages between psychosocial and neurological issues, such as the different impacts of depression. Therewith, the special structure of the CompNet database with its extensive psychosocial and clinical data will be utilised.

### **Research on children and pregnancy**

The western industrialized countries generally achieved reasonable standards for the treatment of HIV positive patients. However, there are differences in the access to treatment and its outcome among certain groups of patients. In particular, HIV infected women and children are disadvantaged. Since they have always been underrepresented in clinical trials, the knowledge about the outcome of antiretroviral therapy in women and children is inadequate. For instance, the characteristics of therapy side effects appear to be different in men and women or in adults and children. An additional disadvantage for children is the inferior availability of antiretroviral

drugs, because not all licensed drugs have approvals for the treatment in children. So there is an urgent need for more knowledge about safety and effectiveness of HIV therapy in women and children. It is also a global challenge since almost half of the HIV infected adults are female and there are about five million children living with HIV/AIDS today.

The CompNet's patient cohort offers all possible opportunities to provide a major part of the essential data needed to answer the named questions prospectively. A special strength are the specific cohort modules on children and pregnant women, reflecting the specific needs of these patients. Interdisciplinary collaborations of various centres guarantee maximal diversification in the management of the relevant issues.