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A decade of follow-up and therapeutic drug monitoring in HIV-2 immunocompromised patientsat St Camille and General Lamizana Military Medical Centers, Burkina Faso, West Africa

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Although HIV-2 is generally less pathogenic than HIV-1, and its progression towards AIDS occurs less frequently. HIV-2 remains an important cause of disease in West Africa, where it is endemic. This study aimed to evaluate HIV-1 and HIV-2 prevalence among pregnant women and to describe the demographic and clinical profile of patients with HIV-2 infection from 2003 to 2013 at St Camille and General Lamizana Military Medical Centers. A retrospective investigation was conducted using 12,287 medical records from patients screened for HIV. To respond to the lack of data available regarding HIV-2 treatment and also to address the approach to clinical, biological as well as therapeutic monitoring, 62 HIV-2 infected patients' medical records were studied. Seroprevalence of 10.6% and 0.14% were obtained respectively for HIV-1 and HIV-2 among 12,287 women screened during the study period. From the sixty two (62) HIV-2 patients, the average age was 49.2 years (sex ratio was 0.65). The weight loss and diarrhea were the major clinical manifestations observed, respectively 54.8% and 25.8%. Fungi and herpes zoster (shingles) infections were reported as major opportunistic infections. Also, nearly half of the patients had more than 60 kg, less than 2% were in WHO stage IV and about 2/3 had a CD4 count bellow 250 cells/mm3. AZT-3TC-IDV/LPV/R was the most prescribed combination. The gain in weight, the improvement of the body mass index (BMI) and the non-significant increase of the rate of CD4 between 1st (M1) and 24thmonth (M24) were observed after treatment with antiviral.

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HTLV-1-infected CD4+ T-cells display alternative exon usages that culminate in adult T-cell leukemia

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Reprogramming cellular gene transcription sustains HTLV-1 viral persistence that ultimately leads to the development of adult T-cell leukemia/lymphoma (ATLL). We hypothesized that besides these quantitative transcriptional effects, HTLV-1 qualitatively modifies the pattern of cellular gene expression. Exon expression analysis shows that patients' untransformed and malignant HTLV-1+ CD4+ T-cells exhibit multiple alternate exon usage (AEU) events. These affect either transcriptionally modified or unmodified genes, culminate in ATLL, and unveil new functional pathways involved in cancer and cell cycle. Unsupervised hierarchical clustering of array data permitted to isolate exon expression patterns of 3977 exons that discriminate uninfected, infected, and transformed CD4+ T-cells. Furthermore, untransformed infected CD4+ clones and ATLL samples shared 486 exon modifications distributed in 320 genes, thereby indicating a role of AEUs in HTLV-1 leukemogenesis. Exposing cells to splicing modulators revealed that Sudemycin E reduces cell viability of HTLV-1 transformed cells without affecting primary control CD4+ cells and HTLV-1 negative cell lines, suggesting that the huge excess of AEU might provide news targets for treating ATLL. Taken together, these data reveal that HTLV-1 significantly modifies the structure of cellular transcripts and unmask new putative leukemogenic pathways and possible therapeutic targets.

Biography

Franck Mortreux has completed his PhD from Paris 6 University (France) and Postdoctoral studies from Agronomy Universirty of Gembloux (Belgium). He is PI in France in the Ecole Normal Superieur de Lyon (UMR5239, LBMC). His researches are mainly focused on HTLV-1 infection and on molecular mechanisms underlying post-transcriptional modifications, virus persistence and oncogenesis.

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