1 PUBLISHABLE SUMMARY

1.1 Project context and objectives

Renal cancer currently accounts for ~3% of adult malignancies worldwide (300,000 new cases out of approximately 11 million), and it is particularly prevalent in some parts of the EU where it is the 10th most common cancer overall[1]. Over 80% of renal cancers are renal cell carcinomas (RCCs).
The CAGEKID project is proposing a comprehensive investigation of genetic and epigenetic changes and resultant downstream proteomic changes in the most common form of renal cancer, renal cell carcinoma (RCC).This is in order to obtain new biological markers that will give better understanding of the disease aetiology, provide new diagnostic and prognostic tools, and lead to new therapies.

The approaches proposed for CAGEKID are motivated by the advent of new technologies and associated methodologies to analyse DNA variation and gene expression on a genome-wide basis. The project will undertake complete analysis of somatic and constitutional DNA variation, methylation patterns and expression in at least 100 constitutional/tumour pairs (as a first stage towards full analysis of 500 pairs).

Existing clinical and epidemiological networks will be mobilised to obtain a minimum of 2250 additional incident kidney cancer sample pairs for follow-up of potential disease markers. The samples will be extensively annotated with clinical and epidemiological data so that these variables can be analysed conjointly with the genomic data. The CAGEKID data will be open to the scientific community and maintained in archives at the European Bioinformatics Institute. The data will also be contributed to the ICGC following the guidelines that will be adopted by the international consortium.

Significant advances in sequencing technology are expected during the course of the programme that may allow increasing the number of fully characterised samples pairs. Standardised collection and sample preparation protocols will be implemented for patient recruitment and sample selection. Training in methodology used in CAGEKID and information on the results will be of interest to a wide scientific and medical public. The diffusion of the methods and results will be assured in a series of training workshops organised and led by the consortium partners.

1.2 Project status at M12

The CAGEKID project was initiated in March 2010. The first year has focused on establishing annotated collections of tumour and constitutional samples of clear cell renal cancer for the study, and undertaking the primary genomic characterisations. Principal results in the first 12 months can be summarised as follows:

1. The establishment of a European-wide network for collecting renal cancer patients and validating the pathology. The network is co-ordinated with ICGC, and meets on the ICGC requirements for pathology and clinical reporting;
2. Development of a prototype of a sample/phenotype repository (KIDREP) to maintain the annotated datasets for renal cancer;
3. Definition of standard operating procedures for nucleic acid extraction and other sample preparation;
4. Identification of ethical and legal issues associated with the project, and review to assure that samples are obtained from patients in concordance with all applicable laws and that appropriate consent and other approval has been obtained for all samples entering the study;

[1] (Ferlay J, Bray F, Pisani P, Parkin DM (Eds.; 2004) Globocan 2002 – Cancer Incidence, Mortality and Prevalence Worldwide (IARC CancerBase No. 5, version 2.0). Lyon: IARC)

5. Application of the above to obtain samples from more than 100 patients meeting inclusion criteria, of which 45 have already gone through sequencing and other genomic characterisation;

6. Development of a rapid validation scheme of the results obtained with these 45 samples so as to confirm potential biomarkers for renal cancer at an accelerated pace compared to original project projections.

Overall, the programme is on target to meet its objectives within the project period.

1.3 Expected final results and their potential impacts and use

CAGEKID brings clinical and epidemiological resources together with the necessary genetics and genomics expertise across Europe to make a major contribution to international efforts to decipher the cancer genome. The results are addressing presently unmet needs for biological markers in renal cancer, which is one of the few cancer sites in which such markers are not yet available for clinical use. Adopting a European-wide approach furnishes us with ability to obtain the clinical collections and biological resources for these studies, which are not available within any single country. This also provides a valuable opportunity to examine the relationship of the variable incidence of the disease in Europe. CAGEKID addresses the specific issue of the FP7 call by structuring EU participation in the ICGC. The consortium is identifying and addressing societal and ethical issues associated with modern genomic studies of cancer. An additional and important contribution of the project will be in the development and diffusion of methodologies and bioinformatics tools for studies involving whole-genome resequencing, and related techniques.

Consortium

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Partners:

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2. International Agency for Research on Cancer (IARC)
3. Charles University of Prague, First Faculty of Medicine, Institute of Hygiene and Epidemiology (CU-IHE)
4. Department of Epidemiology and Prevention, Russian N.N.Blokhin Cancer Research Centre and Russian Cancer Society (RCS-CRC)
5. European Molecular Biology Laboratory, European Bioinformatics Institute (EMBL-EBI)
6. Karolinska Institute/ Karolinska University Hospital (KI)
7. Center BioEngineering, Russian Academy of Sciences (CB)
8. Cancer Research UK Centre, University of Leeds, UK (UNIVLEEDS)
9. Royal Institute of Technology (KTH)
10. Centre National de Génotypage, Institut Génomique, Commissariat à l'Energie Atomique (CEA-CNG)
11. Institut National de la Santé et de la Recherche Médicale (INSERM)
12. Institute of Mathematics and Computer Science (IMCS)
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