The Molecular *In Silico* Dissection of Cancer using TCLASS® and its Application in the Identification of the Tissue of Origin of Cancers of Unknown Primary Site

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Introduction

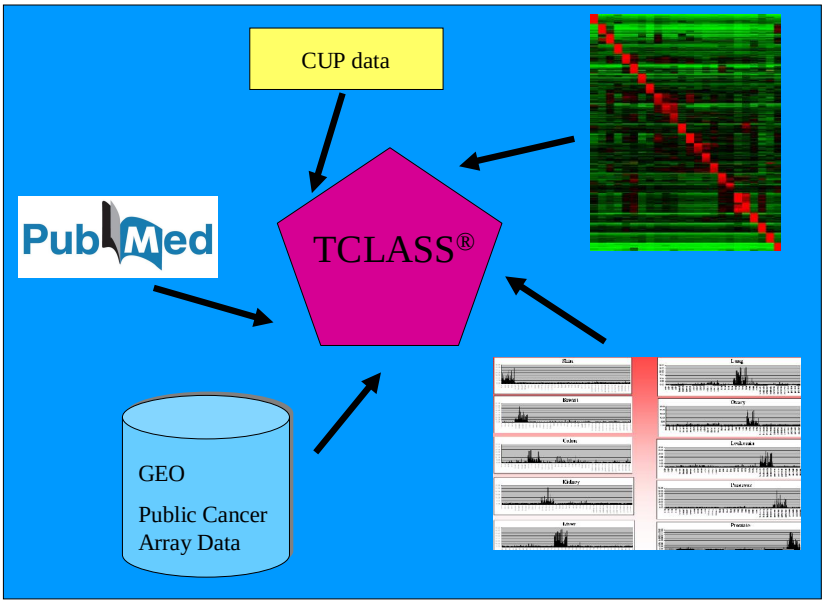
Traditional cancer diagnosis relies on a combination of clinical and histo-pathological data. In many cases, however, the morphology of in particular metastatic cancer is not discriminative enough for correct diagnosis. In addition, the morphology of tumor cells do not provide information on aberrant molecular pathways that may be used to specifically target the tumor like the application of Herceptin to breast cancers with amplification in the ERBB2 gene. With the completion of the human genome project, molecular pathology has dramatically increased its arsenal of novel molecular biomarkers that can be used to determine the phenotype of tumors. Gene expression profiling using high-density microarray technology is an extremely powerful tool to comprehensively characterize the tumor phenotype. We have developed TCLASS® a multi-class tumor classifier that interprets gene expression microarray data and allows the identification of the primary site of Cancers of Unknown Promary site (CUP). The classifier is implemented as a web-based tool and is an extremely simple and straightforward approach for molecular characterization of tumor samples. We are currently looking for collaborations with clinicians with access to fresh frozen CUP samples to further validate the tool in a clinical context. Alternatively, CEL files of CUP samples analyzed with Affynetrix 133 Plus 2.0 arrays can also be directly analyzed using TCLASS.

Features of TCLASS®

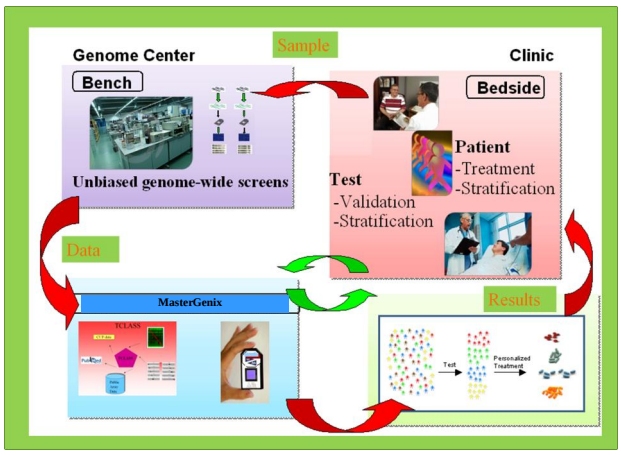
- **-Molecular Multi-Class Tumor Classifier**
- **-Based on differential gene expression**
- **-Many data sets have been used**
- **-Successive iterative rounds of independent validation**

Advantages of Molecular Classifier

- **-Assay is standardized and robust**
- **-Amendable to automation**
- **-Independent of local expertise of pathologist**
- **-Potential for being more reproducible at international multi-center level**



Our gene expression microarray-based method helps determining the site of origin of more than 40 subtypes of metastatic cancer. It provides information on the level of infiltrating immune or stromal cells and also provides scores for proliferative capacity, carbohydrate consumption and many relevant targets useful to clinicians for the determination of a personalized targeted (antibody-based) treatment or a tailored chemotherapeutic regimen for the individual patient.



Conclusions

Implementation of TCLASS should result in significant cost savings and an improved diagnosis of the site of origin of metastatic cancers of unknown or uncertain origin. Diagnostic molecular pathology should be of potential clinical use in determination of the optimal treatment regime of metastatic cancer. We are looking forward to collaborate with clinicians for the further validation of this tool.