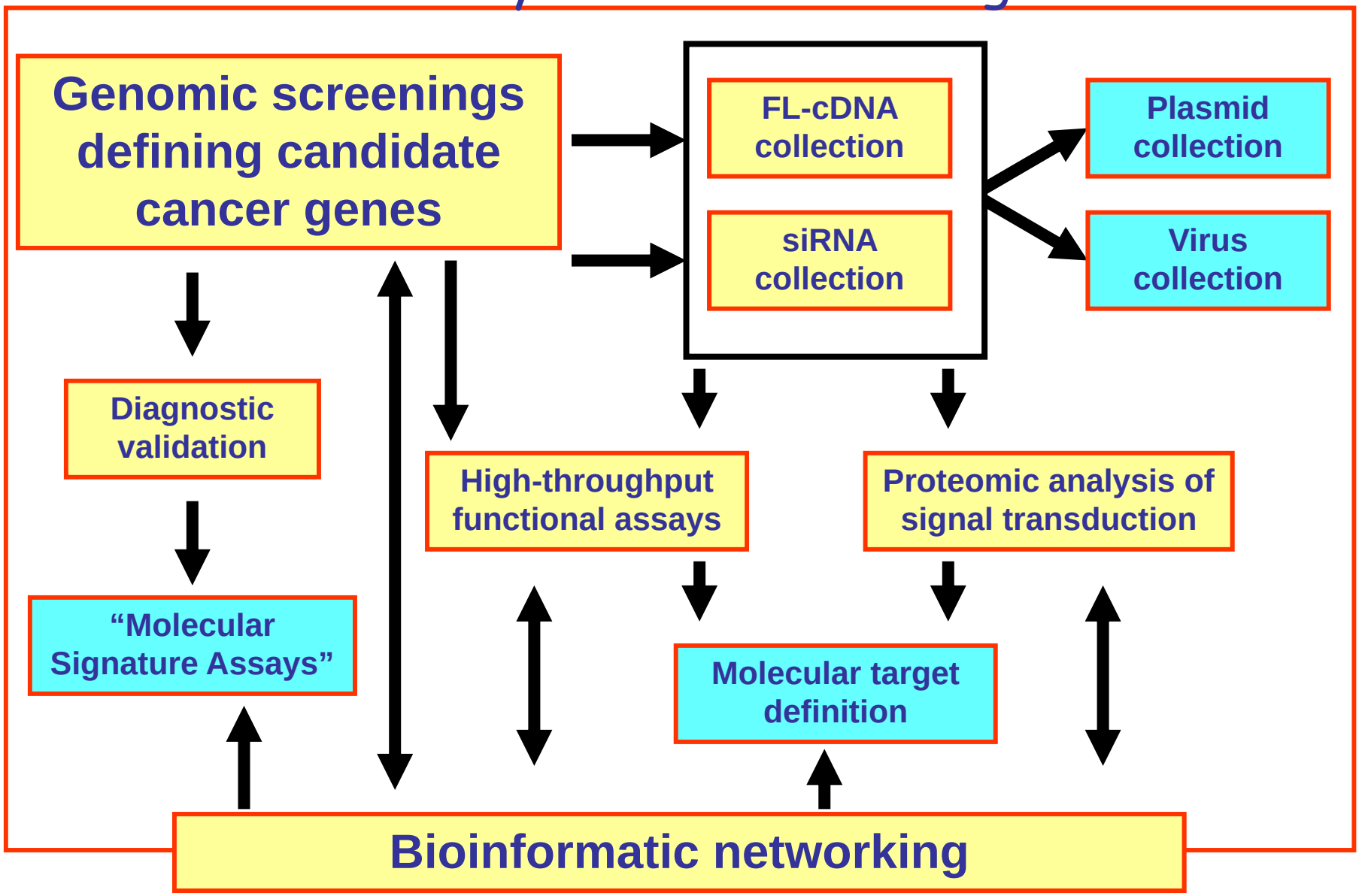
A European Sixth Framework Integrated Project

Translational and Functional Onco-Genomics: from cancer-oriented genomic screenings to new diagnostic tools and improved cancer treatment.

The TRANSFOG Plan for High-Throughput Functional Analysis of Cancer Progression



Participants

Partner	Organisation Name (short name)	Scientific Team Leader
P1 (Admin. Coordinator)	Organization of European Cancer Institutes (OECI)	Guy Storme
P2 (Scient. Coordinator)	Institute for Cancer Research and Treatment (IRCC)	Enzo Medico, Paolo Comoglio
P3	Spanish National Cancer Institute (CNIO)	Mariano Barbacid
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P5	Netherlands Cancer Institute (NKI)	Rene Bernards
P6	University Medical Center Utrecht (UMCU)	Johannes L. Bos
P7	FIRC Institute of Molecular Oncology (IFOM)	Marco Pierotti
P8	European Molecular Biology Laboratory (EBI)	Rolf Apweiler
P9	Biomed. Sciences Research Centre “Alexander Fleming” (Fleming)	George Panayotou
P10	Friedrich Miescher Institute for Biomedical Research (FMI)	Nancy Hynes
P11	Agendia BV (Agendia)	Bernhard Sixt
P12	University of Innsbruck Institute of Pathophysiology (IPP)	Stephan Geley
P13	Karolinska Institute (KI)	Edvard Smith
P14	Ludwig Institute for Cancer Research - UCL Branch (LICR-UCL)	Anne Ridley
P15	Ludwig Institute for Cancer Research –Uppsala Branch (LICR-UPP)	Carl-Henrik Heldin
P16	National Interuniversity Consortium Laboratory (LNCIB)	Claudio Schneider
P17	Max-Delbrueck-Center for Molecular Medicine (MDC)	Walter Birchmeier
P18	The Weizmann Institute of Science (WIS)	Yosef Yarden

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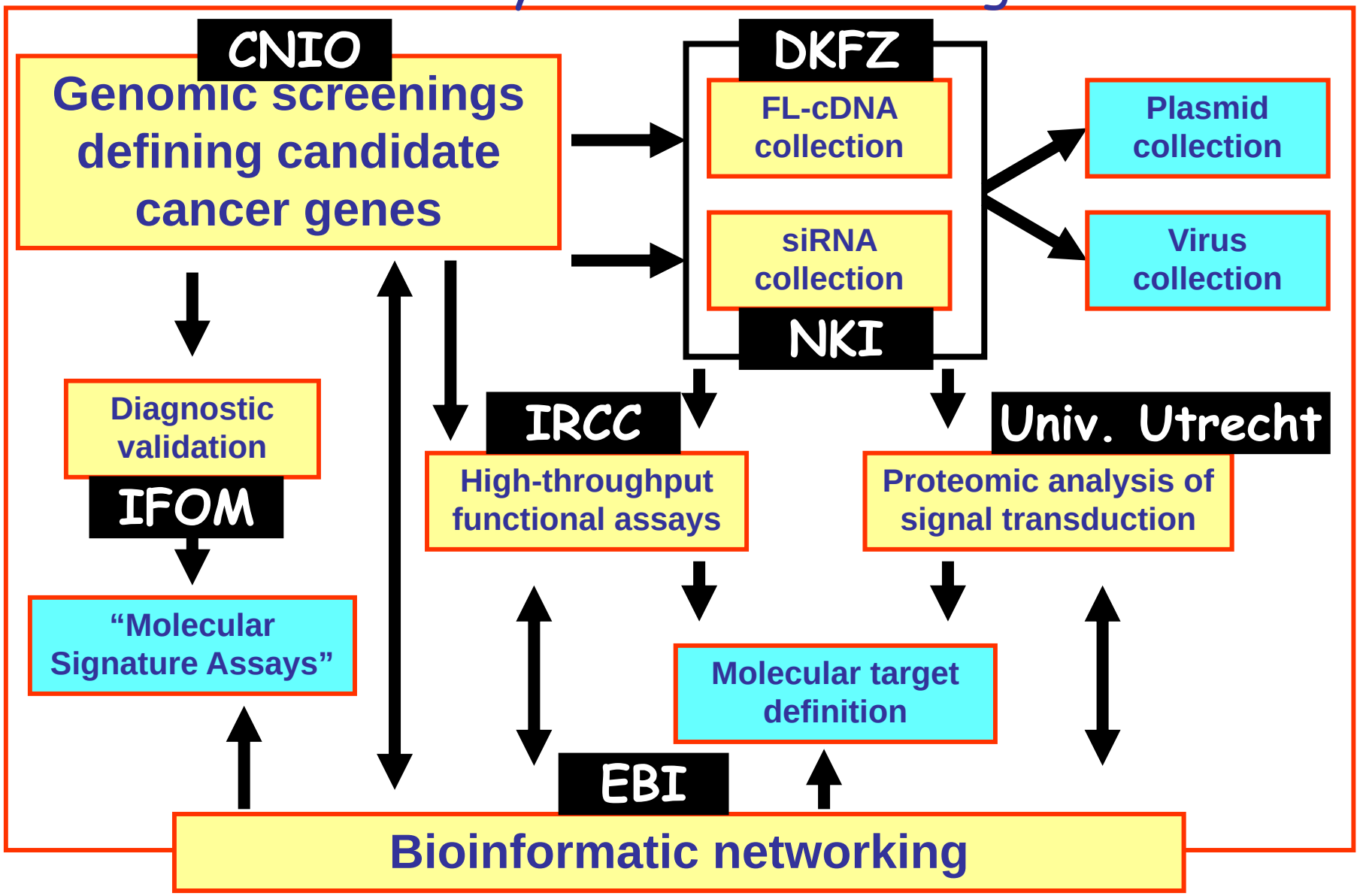


Project Phases

- Phase I (2005): Initial set-up of experimental procedures for systematic cancer gene functional analysis and clinical validation; establishment of standards and tools for data sharing and mining.
- Phase II (2006-2007): Systematic gene functional analysis and diagnostic validation of new cancer molecular signatures.
- Phase III (2008): collection of results, dissemination of technologies and deliverables to the European cancer research community and cancer hospitals. Exploitation of the achieved results, mainly as new cancer diagnosis tools and screening targets for new cancer drug discovery.

Cell-based screenings

Partner	Screening model
IRCC	Microarray analysis of genes regulated by HGF, EGF and semaphorins in normal and neoplastic, human and mouse cells.
UMCU	Microarray analysis of tumour cell lines after stimulation or inhibition of the Ras, the Akt/PKB and Wnt pathway.
LICR-UCL	Proteomic analysis of ErbB-2-dependent changes in protein expression in immortalized human mammary luminal epithelial cells (HuMLECs)
LICR-UPP	Microarray analysis (Affychips) of PDGF- or TGFbeta-stimulated normal and cancer cells.
LNCIB	Microarray analysis of tumour cell lines after stimulation or inhibition of the p53 and beta-catenin pathways.
WIS	Gene expression profiling of Erb-B negative feedback loops driven by Erb-B negative regulators in human cancer cell lines.

Target gene functional analysis in cell-based systems

Partner	Functional assay
IRCC	Scattering, angiogenesis, morphogenesis, transformation and invasion of cultured epithelial and endothelial cells.
CNIO	Epigenetic functions (DNA methylation levels).
NKI	Escape from senescence.
UMCU	Reporter gene expression responsive to the Ras, PKB/Akt and Wnt pathways.
FMI	Mammary tissue function: proliferation, migration, and differentiation.
IPP	Apoptosis assays in neopastic cells
KI	Growth and apoptosis in neoplastic cell lines
LICR-UCL	Cell migration, cell-cell adhesion and transmigration of cancer cells across endothelial cells.
LICR-UPP	PDGF and TGF-beta signaling in cell growth, chemotaxis, actin reorganization, and invasiveness.
LNCIB	Apoptosis, proliferation, cell cycle, morphology, motility, adhesion.
WIS	Negative regulation of ErbB RTK signaling, proliferation and survival; modulation of ErbB2 stability.

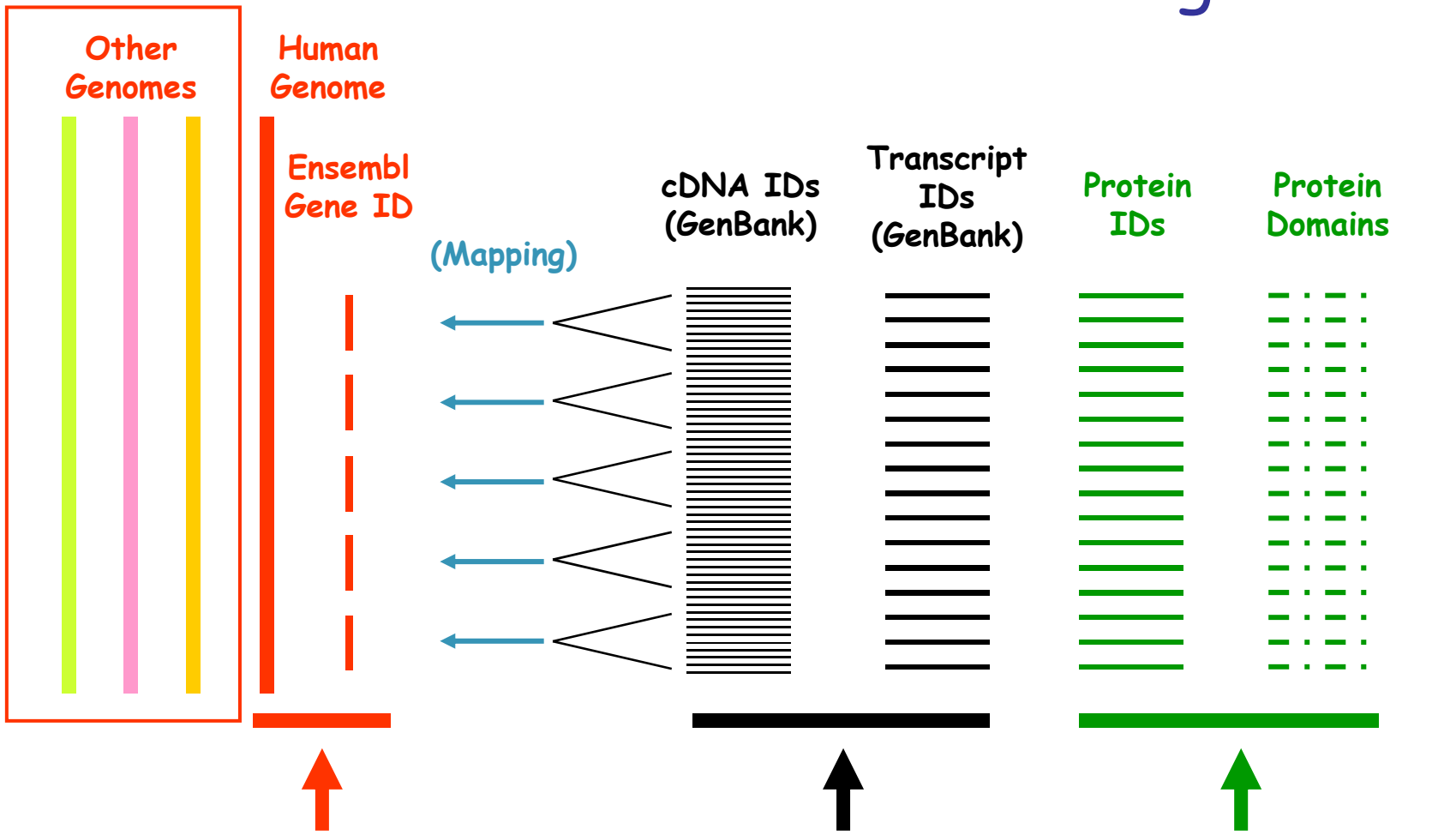
Target gene validation in in vivo systems

Partner	Experimental model
CNIO	Creation of genetically modified mice (transgenic, knock-out, knock-in)
FMI	Mouse mammary gland reconstitution
LICR-UCL	Parameters of cancer progression in Drosophila cells
MDC	Assays in lower organism systems (Drosophila and zebrafish)
LICR-UPP	PDGFR-based tumor model in mice

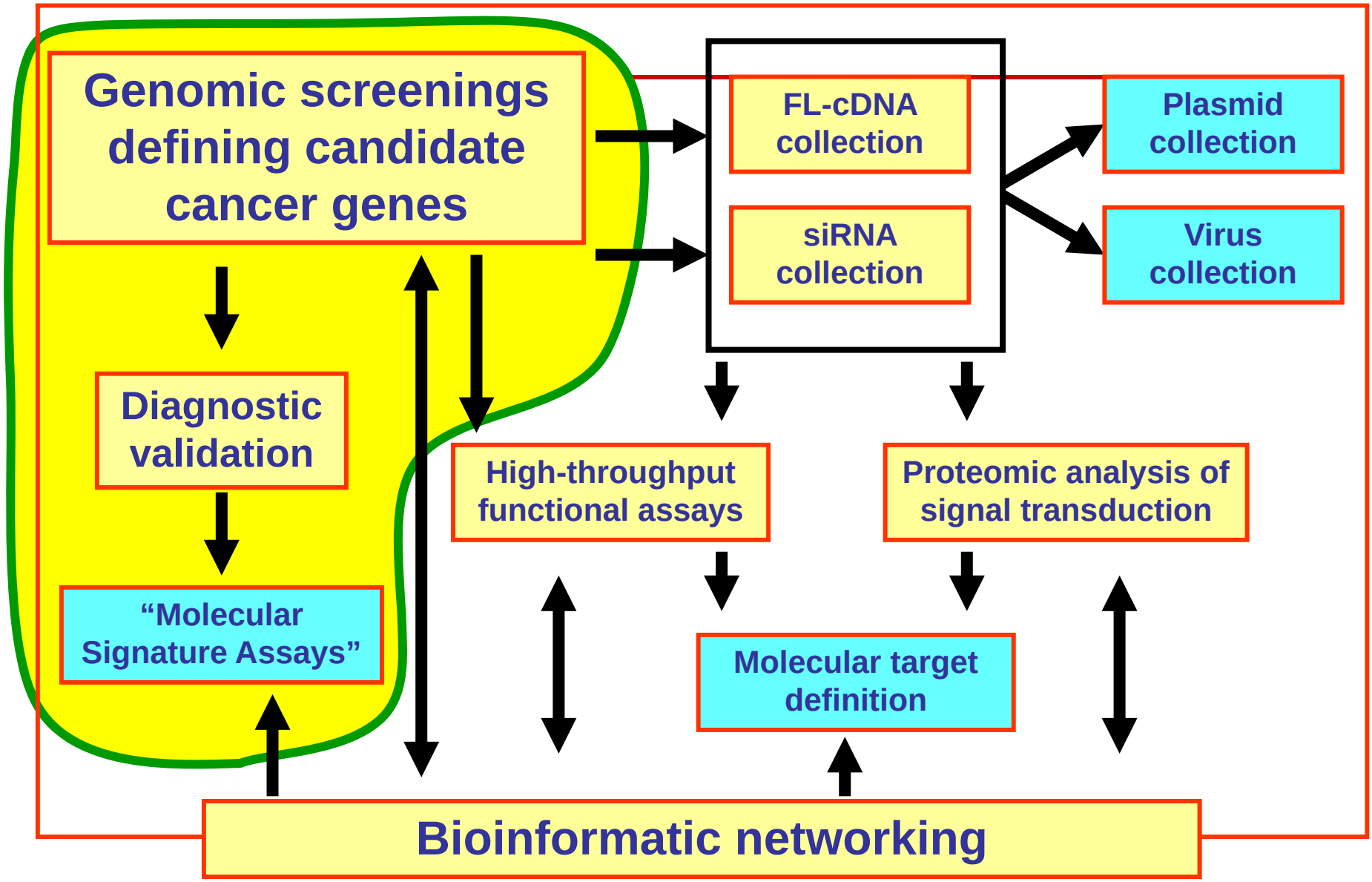
Tumour-based screenings

Partner	Screening model
CNIO	Microarray, CGH and epigenetic analysis focussed on metastatic progression of breast, lung and colon cancer.
IFOM	Microarray analysis in breast and lung cancer, in particular to identify those N0 tumours that have a higher risk of metastasising.
Agendia	Gene expression profiling of colon cancer using 25,000 human oligonucleotide microarrays.
LNCIB	cDNA microarray analysis of colon cancer samples, with a specific focus on signaling pathways (FGF and TGFß, invasive ovarian cancer) and hereditary background
MDC	Affychips on colon cancer: a) metastatic and non-metastatic primary tumours, b) metastatic primary tumours and their metastases, and c) metastases to different target organs.

Data Standardization and Integration



OECI members can play a role in TRANSFOG



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Thank You!

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