Project no.
037472

Project acronym
TAMAHUD

Project title
Identification of early disease markers, novel pharmacologically tractable targets and small molecule phenotypic modulators in Huntington's Disease

Instrument: **STREP**

Thematic Priority: **LSH-2005-2.1.3-8: Early markers and new targets for neurodegenerative diseases – STREPs dedicated to SMEs**

Title of report

Final activity report

Period covered: **January 1st, 2007 - December 31st, 2010** Date of preparation **February 22nd, 2011**

Start date of project: **January 1st, 2007** Duration: **42 Months**

Project coordinator name: **Dr. Andrea Caricasole**
Project coordinator organisation name: **Siena Biotech SpA**

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Project execution

Overview of general project objectives

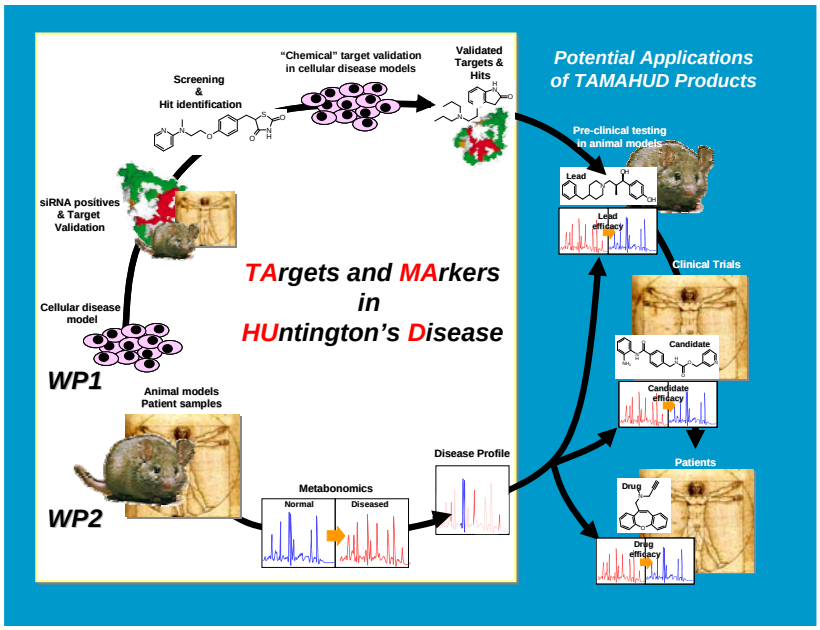
TAMAHUD addresses the Call Section "LSH-2005-2.1.3-8: Early markers and new targets for neurodegenerative diseases". Huntington's disease (HD) is a devastating neurodegenerative disease with significant unmet patient needs. There are no known ways of slowing or preventing the neurodegeneration, and clinical trials in man are hampered by the slow disease progression and the absence of suitable biomarkers of short-term progression. The genetics of HD is characterized by, and involves the expansion of a polyglutamine tract at the amino-terminus of the Huntingtin gene (HTT). However, the translation of this knowledge into therapeutic and diagnostic approaches is hampered by the limited knowledge of HTT biology, the paucity of information on how cellular signalling pathways interact with the HD mutation, and the lack of systematic and modern approaches aimed at identifying useful biopredictors of disease progression in individuals diagnosed with HD. TAMAHUD addresses key areas of HD patient need, namely the discovery and development of therapeutically meaningful novel targets and biomarkers. The complementarity of the two objectives of TAMAHUD (target & lead discovery and biomarker discovery) is underscored by the need for therapeutically relevant lead compounds and for reliable means of assessing efficacy in both pre-clinical and clinical settings through the use of appropriate biomarkers. Ultimately, TAMAHUD aims at delivering active lead molecules for further development and candidate biomarkers for clinical validation.

Consortium composition

The consortium is composed of an SME (Siena Biotech SpA) coordinating the activities of 2 academic (University of Cambridge and the European Molecular Biology Laboratory) and 2 SME partners (Total Scientific Ltd and BioAlma SA). 4 European countries are represented (Italy, Spain, UK and Germany). Siena Biotech SpA, Siena, Italy, (**SIBI**) provides the drug discovery expertise and technological platforms (including relevant Bioinformatics aspects) required to progress the discovery and development of small molecule therapeutics, which constitutes the driver of WP1 activities. HD is one of the 2 neuroscience disease areas where SIBI has its own active drug discovery project. Therefore, the drug discovery expertise which is provided by the coordinator is also highly relevant for TAMAHUD. SIBI has also been in charge of providing the cellular disease model for the HT-RNAi screen, subcontracted to a specialist SME (CENIX GmbH, Germany), for supervising such activities and for delivering the list of targets from such screen for selection within the consortium. The University of Cambridge, Cambridge, UK (**CAM**), represented by Prof. D. Rubinsztein, provides the target validation support for WP1 as well as relevant supporting and supervision activities required for WP2. The internationally acknowledged expertise in the biology and molecular genetics of HD as well as the significant clinical experience provided to TAMAHUD by Prof. Rubinsztein are clearly a key asset to the context and objectives of TAMAHUD. Total Scientific Ltd (**TSL**), a UK based SME, provides the expertise in metabonomics studies and replaced TCP innovations (TCP) in the course of the reporting period. TSL is engaged in WP2 activities, and is supported in this by CAM. The European Molecular Biology Laboratory, Heidelberg, Germany (**EMBL**), is contributing data integration and bioinformatics support to both workpackages. BioAlma SA, Madrid, Spain (**BAL**), contributes text mining expertise in order to ensure unbiased and systematic knowledge coverage and mining of any published information relevant to targets/metabolites identified in TAMAHUD, in order to explore direct/indirect associations with HD or with other neurological disorders bearing similarities to HD.

Experimental strategy

The two objectives (novel drug targets and biomarkers) are pursued in the two workpackages (WPs) in which TAMAHUD is organized (see figure below). In WP1, High throughput-RNAi, focusing on genes encoding pharmacologically tractable proteins has been employed within a novel and robust HD cellular disease model to identify genes whose inhibition of expression is protective against the HD mutation. At the end of the first reporting period, a number of such targets have been identified that satisfy the criteria for progression to further target validation activities. Following these target validation activities, at least two targets are to be selected for assay development and primary screening activities, to identify drug-like compounds active on the target and efficacious against the HD mutation in cellular disease models. In parallel, in WP2, the biomaterial repository made available to the consortium from CAM is being investigated by TSL through state-of-the-art metabonomics approaches to identify biomarkers predictive of disease onset and progression.



Potential Impact

The key unmet needs in HD are the lack of effective therapy currently available to patients, resulting from the limited understanding of the molecular mechanisms associated with the pathological consequences of the HD mutation, and the lack of easily accessible, rapid and predictive biomarkers for monitoring disease onset/progression in pre-clinical and clinical studies. TAMAHUD promises to deliver a significant impact on:

- the understanding of the molecular mechanisms underlying HD-relevant phenotypes in a cellular disease model through the functional identification of targets capable of modulating such phenotypes (WP1);
- ...drug discovery based on these targets aimed at aimed at identifying hits/leads to be developed into small molecule therapeutics (WP1);
- the identification of biomarker profiles predictive of disease onset/progression for further clinical validation (WP2).

These potential applications of TAMAHUD deliverables are illustrated in the figure above, and can be summarized into A) chemical leads for development into disease-modifying therapeutics and B) metabolite profiles for development into diagnostics of disease onset/progression. TAMAHUD does not extend to the validation of identified small molecule hits in animal disease models since such activities form part of the hit-to-lead phase of drug discovery and their implementation cannot be reasonably expected within the envisaged timelines and resourcing. However, TAMAHUD aims to culminate its activities in the constitution of a solid base for the later completion of pre-clinical development of potential drugs, comprising the demonstration of in vivo efficacy of TAMAHUD-derived chemical series in part through the use of TAMAHUD-derived biomarkers. Subsequent clinical studies on candidate drugs originating from TAMAHUD activities will again benefit from the inclusion of TAMAHUD biomarkers to determine clinical efficacy.

Contractors Involved

Participant Role*	Participant Number	Participant name	Participant short name	Country	Date enter project**	Date exit project**
CO	1	Siena Biotech SpA	SIBI	Italy	1	42
CR	2	University of Cambridge	CAM	UK	1	42
CR	3	TCP Innovations	TCP	UK	1	1
CR	4	Alma Bioinformatics S.L	BAL	Spain	1	42
CR	5	EMBL Heidelberg	EMBL	Germany	1	42
CR	6	Total Scientific	TSL	UK	1	42

Coordinator details

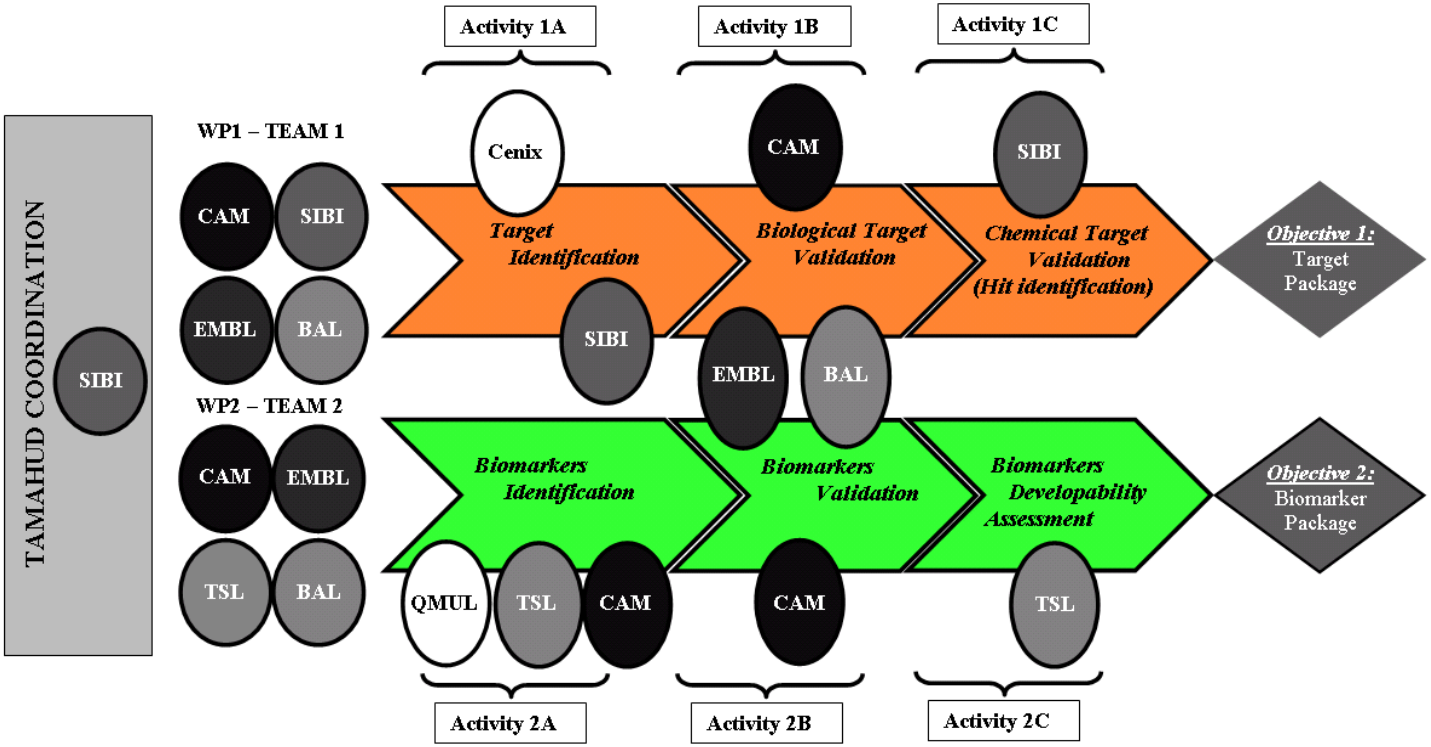
Andrea Caricasole, PhD
Siena Biotech S.p.A.
Strada del Petriccio e Belriguardo 35
53100 Siena - ITALY
Tel: (+39) 0577 381 307
Fax: (+39) 0577 381 303
acaricasole@sienabiotech.it

Project Logo

Web site address

www.tamahud.eu

Project general workflow



Project objectives and major achievements

TAMAHUD's general objectives have been organized into two workpackages (WPs), each addressing the interdependent unmet needs of HD patients of a) the understanding of the mechanisms associated with the toxicity of the HD mutation, with the purpose of developing disease modifying therapeutics (WP1) and b) the identification of biomarkers (metabolites) of disease onset/progression for the development of diagnostics (WP2). The two workpackages were supported by a strong bioinformatics and *in silico* biology platform, enabling immediate comparison and contextualization of results with publicly available literature and datasets. Each WP comprised clear, logically connected, intermediate objectives, deliverables and go-no go decision points, which are described in detail in the subsections below. As a general statement of achievements, TAMAHUD in the course of its life has produced several druggable targets functionally associated with the toxicity induced by the HD mutation in mammalian cell disease models as well as in a Drosophila disease model, whose inhibition of expression (which may be phenocopied by pharmacological inhibition) results in amelioration of phenotypes. Aside from a significant contribution to disease understanding, enhanced by the bioinformatics analysis of associated pathways and literature datasets, these targets have been progressed to screening activities for the development of small molecule modulators, and hits have been identified which can be further developed into leads and candidate compounds in follow-up activities. In parallel, cross-sectional and longitudinal metabolite profiles have been generated in peripheral (blood) samples from both HD patients as well as transgenic mouse models with the aim to allow a comparative analysis of potential markers of disease progression with translational potential, which upon further validation in follow-up studies may aid the development of candidate drugs.

Workpackage 1: target identification and validation

WP1 Objectives.

Identification, validation and exploitation of novel pharmacological targets for the modulation of mutant HTT-associated phenotypes. In spite of the monogenic nature of HD and the nearly 40 years of knowledge since the nature of the mutation was discovered, there are still few developments in terms of therapeutics. There is a clear need to identify molecular mechanisms associated with the phenotypic effects of the HD mutation and in particular to identify molecular targets amenable to pharmacological intervention and exploitable for drug development. In WP1, TAMAHUD aimed to identify and validate new targets whose modulation could revert HD-associated phenotypes in preclinical models and to develop screening programmes to identify small molecule modulators with potential for future development into pharmacological therapies.

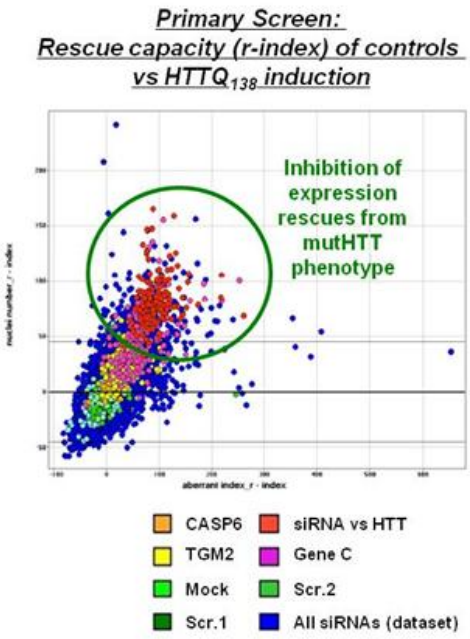
Contractors involved, work performed and end results (elaborating on the degree to which the objective were reached)

An approach towards the identification of druggable protein targets of potential relevance to disease modification is to sample in an unbiased way the so called "druggable genome" for genes whose downregulation of expression can alter a human disease-relevant phenotype in a preclinical disease model. The rationale being that inhibitors of some protein target's activity (be it an enzyme, a G-protein coupled receptor, an ion channel or a nuclear receptor, to name the most studied druggable

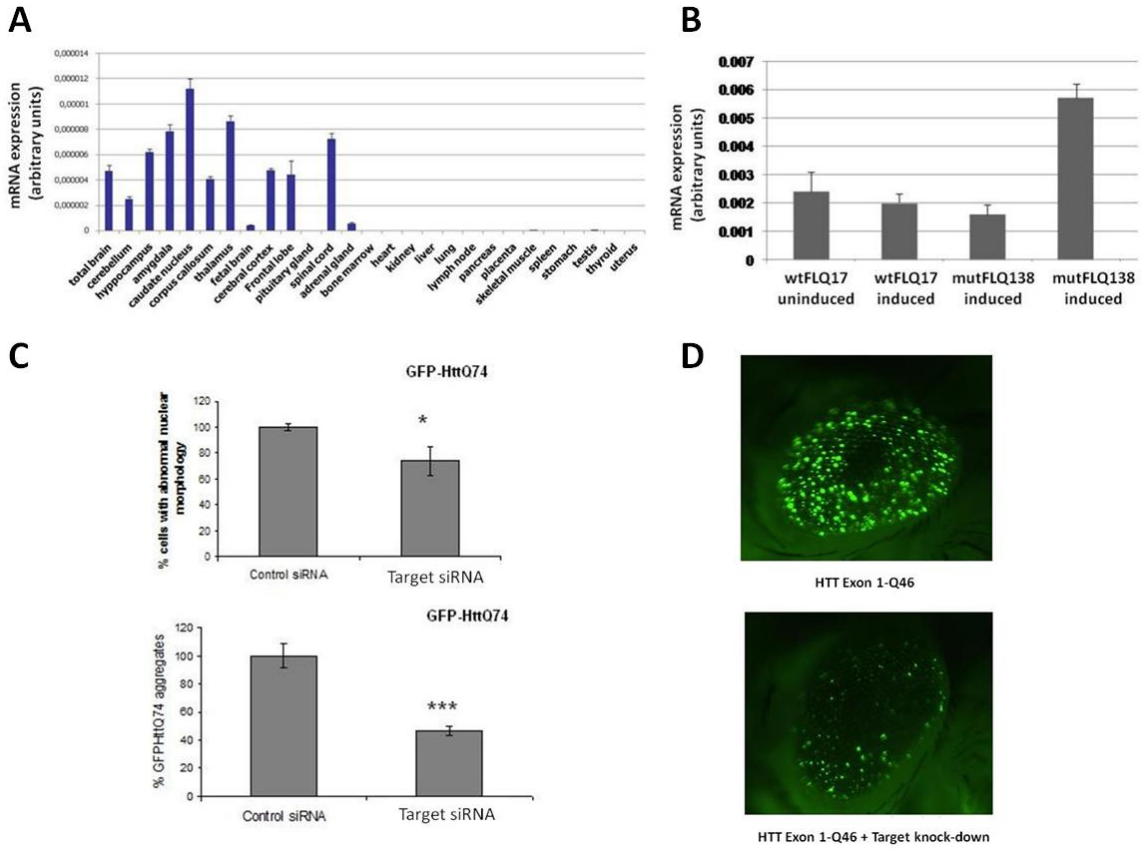
protein classes) are usually easier to develop than positive modulators/agonists/activators. The druggable genome represents that subset of the human genome encoding proteins for which there is either empirical evidence (typically, from Pharma/Biotech industry experience) that the target can be pharmacologically modulated with a small chemical entity, or for which potential binding pockets for small molecules have been identified. It is still a relatively large set of genes (more than 5000), and its functional analysis therefore imposes practical constraints on the nature of the disease model to be employed and typically makes use of collections of siRNAs/shRNAs (for RNAi screens) or cDNA expression vectors (for overexpression screens) covering the corresponding gene set. In the case of TAMAHUD, the rationale was to identify genes encoding druggable proteins whose downregulation of expression in a disease model could revert the phenotypes associated with the HD mutation. Preclinical disease models represent useful experimental tools for the modelling and manipulation of aspects of the human pathology. In a screening context, the disease model needs to represent aspects of the human pathology and at the same time provide the robustness, reproducibility, ease of manipulation and scalability required for the simultaneous manipulation and analysis of large numbers of individual data points. In order to reach a necessary compromise between practical aspects of screening these large numbers of siRNAs and the physiological relevance of the disease model, a human cell line inducibly expressing a human full length, mutant HTT transgene was characterized and chosen **(Partner 1)**. In this cell line, induction of transgene expression leads to a decrease in cell numbers as compared to uninduced controls or cell lines of identical background in which expression of a human full length wild type HTT is induced. The phenotype can be quantified by different means, and a High Content imaging composite readout was chosen allowing the evaluation of cell loss as well as of changes in nuclear morphology characteristic of apoptotic cell death. The screen was outsourced to a specialist CRO (www.cenix-bioscience.com). More than 5000 genes were sampled in the screen, whose results are depicted in the figure below. Reference siRNAs, specific for genes whose activity has been functionally linked to the toxicity of the HD mutation in preclinical models (Caspase 6 and Transglutaminase 2), as well as a siRNA specific for the human HTT sequence, were used as positive controls. Positives, colocalizing in the same quadrant of the positive controls, were selected for successive rounds of validation using independent siRNAs.

Primary screen

- 16.869 siRNAs targeting 5623 genes
- 240 plates (384 wells)
- >400.000 images analyzed
- Reference genes from literature, as well as siRNA vs HTT, used as controls
- Successive round of validation using different siRNAs for each positive gene
- QPCR validation of siRNAs effectiveness
- Results: 48 target genes whose RNAi ameliorates phenotype in this model

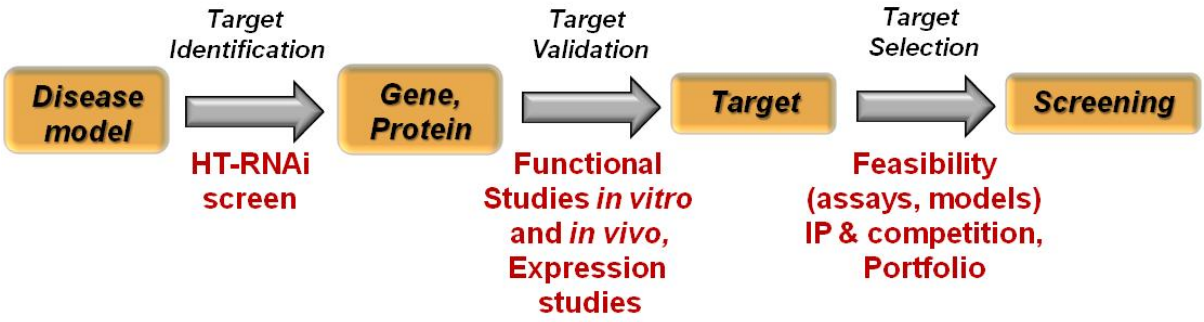


Bioinformatics analysis **(Partners 1, 4, 5)** of primary actives revealed targets associated with a number of pathways previously linked to HD (such as cAMP signalling, cytoskeletal remodelling, cholesterol and glucose metabolism) as well as novel ones. The whole process resulted in a final list of 48 targets which included enzymes, transporters, ion channels and G-protein coupled receptors. A subset of these targets were selected for further validation studies based on the possibility and ease of developing assays, on novelty and on the phenotypic reversion score in the HT-RNAi screen. Further functional validation studies were performed in complementary mammalian cell-based models of HD (expressing the toxic Exon 1 fragment of mutant HTT protein) where reversion from mutant protein aggregation and cytotoxicity through RNAi was sought, as well as in a Drosophila HD model expressing a mutant HTT Exon1 fragment where the effects of genetic knockdown of fly orthologues of the selected genes were scored for reversion of the eye degeneration phenotype **(Partner 2)**. Additionally, the profile of expression of these genes was investigated by QPCR in a comprehensive panel of cDNAs from human tissues, to determine CNS selectivity of expression, and in cell lines inducibly expressing either the human full length wild type or mutant HTT protein **(Partner 1)**. Representative examples of data generated during the target validation process are illustrated below.



In A, a profile of expression in different human tissues of one of the targets is shown, indicating a CNS-restricted profile of expression for this target. In B, an example of the analysis of target transcript expression (QPCR) in mammalian cell lines inducibly expressing full length wildtype (wtFLQ17) or mutant (mutFLQ138) human HTT is depicted, showing that expression of this target is induced selectively upon expression of the mutant full length transgene. In C, the effects on mutant HTT cytotoxicity (top panel) and aggregation (bottom panel) of RNAi on a target in mammalian cell lines expressing an Exon 1 mutant HTT fragment is shown, indicating that interference with this target's expression leads to amelioration of the HD phenotypes in this model. Finally, in D an example of genetic knock-down of a target on mutant Exon1 HTT aggregation in the eye in the Drosophila HD model is depicted, showing that interference with expression of this target ameliorates eye mutant HTT aggregation (and associated degeneration, not shown).

The entire process of target selection for the initiation of screening activities is depicted below.

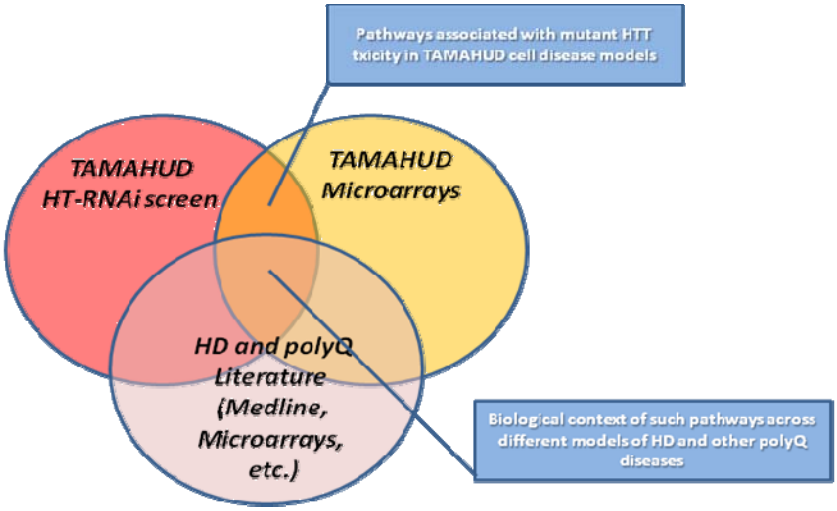


At the end of the validation process, of the several targets that resulted validated in the different preclinical models employed in TAMAHUD, 2 targets were progressed to screening activities **(Partner 1)**, namely a GPCR and an enzyme. The screening campaigns, each involving assay development activities and primary screening of collections with ca. 30.000 compounds each, pre-selected to meet predicted criteria for CNS permeability, resulted in the identification of at least one hit series for each target while further structurally distinct series are currently being validated. Upon further optimization, these molecules will be employed to pharmacologically confirm the targets that have been validated using genetic means, therefore providing a proof-of-concept for their further development. These novel modulators of the targets identified in TAMAHUD represent promising starting points for the development of therapeutics, therefore fulfilling WP1's initial objectives.

Bioinformatics activities

Although formally not a workpackage in itself in TAMAHUD, the Bioinformatics activities supported both workpackages and were especially important in data analysis and contextualization in WP1. Specifically, the Bioinformatics activities within WP1 were expected to support target selection and the investigation of mechanisms underlying the HD phenotype. The hits from the HT-RNAi screen were analyzed in terms of druggability, novelty and pathway involvement **(Partners 1, 4, 5)**: findings guided the HT-RNAi screen progression through successive waves of confirmation and target selection for functional and expression studies from the final list of targets produced from the HT-RNAi screen (48). In summary this first list of targets that underwent validation was mostly composed by GPCRs and enzymes, few ion channels and transporters. Among these almost 20% were previously described in HD as modulated genes or involved in mutant huntingtin toxicity; the pathways associated to these hits are known in HD as cAMP mediated signaling, mitochondrial dysfunction, lipids metabolism, glutamate metabolism, PPAR signaling, BDNF signaling as well as other, not clearly defined pathways such as post-translational modification, cell cycle specific activity. The same proportion was observed in the larger list of hit genes (260) in which both novel and well-known targets were included. Many of these are associated to cAMP, glutamate, mitchondria, lipids, calcium, PPAR, cytokine as well as serotonin signaling, RXR, prothrombin, Wnt and acids signaling. Interestingly, 7 genes associated to the Rock pathway are among the hits, in agreement with the protective effect of Rock inhibition in HD and in models employed for the HT-RNAi screen. Beside the activities for target selection, comparative contextualization of TAMAHUD and public data on HD transcriptional changes and functional screens, and on HTT interactors/modulators **(Partners 1, 4, 5)** was expected to provide a strong basis for deconvoluting the pathomechanisms underlying the HD phenotype and for selecting further targets for future validation studies. Interestingly, 20 % of the top siRNA protective genes are modulated in the same cell model; in particular, 10% are upregulated and might support the evidence from siRNAs of a toxicity associated to over-activity or expression of the genes. Modulated genes and

hits from the TAMAHUD HT-RNAi screen were associated to inositol phosphate metabolism, PPAR and RXR, endothelin, FAK, inflammation mediators (TNF, ILs), mTOR, lipids, piruvate, post-translational modification, and others. These results have been obtained through the integration of different approaches, i.e. text mining, pathway analysis and integration of data from publicly available datasets. These same approaches have been used also for a specific analysis for some of the validated targets.Potential substrates and effectors have also been predicted, representing not only hypotheses for mode of action of these genes but also potential markers of activity. The huge body of data obtained by the bioinformatic analysis of hits and HD literature have been collected in a database developed at EMBL, which allows the comparison between datasets and visualization of pathways and other biological information associated to the genes. The database profits the development of the 'Biocompendium' tool for extraction and integration of data. The overall Bioinformatics approach is depicted in the diagram below, where TAMAHUD datasets are contextualized with published literature on HD and other polyQ diseases using tools developed or adapted within TAMAHUD.



Workpackage 2: Biomarker identification

WP2 Objectives.

Identification, validation and exploitation of novel biomarkers for each gene-positivity and symptom progression.
Such biomarkers should ideally be sought both in the presymptomatic period and in early symptomatic cases, to facilitate assessments of possible therapies.

Contractors involved, work performed and end results (elaborating on the degree to which the objective were reached).

The approach taken to try and identify biomarkers of HD progression was to use metabolomics, the analysis of the small molecule metabolites. Three distinct approaches were taken **(Partner 6)**, using three different sample sets (provided by **Partner 2**): cross-sectional samples from patients with HD

and their controls, longitudinal analysis of samples taken 12 months apart from patients with HD, and analysis of a transgenic mouse model of HD, with samples taken at different ages to represent different stages of the disease.

Initial experiments were performed to optimise the methods used for the metabolomic analysis. Different NMR techniques were tested, as were both chemical and physical protein-removal techniques. These experiments led us to select acquisition of the NMR metabolomics data using the CPMG pulse sequence to edit out large molecules such as proteins, which eliminated the requirement for any chemical or physical processing of the serum. This approach maximises the reproducibility of the technique while minimising the interference of the technique by the very large levels of protein present in the serum samples.

Human HD serum samples were collected from symptomatic as well as presymptomatic patients. Control samples were also collected, primarily from the partners of HD patients. In the first instance (cross-sectional analysis), samples taken at a single time point from both presymptomatic and symptomatic HD patients were compared with control samples. Later analysis was performed using samples from patients collected 12 months following the first sample so that the change in metabolites over the 12-month duration in individual patients could be analysed. In addition, a transgenic mouse model of Huntington's Disease was also utilised.

Serum samples were provided from mice expressing a mutant huntingtin gene and their healthy littermates at 8 weeks of age prior to the development of HD-like symptoms and also at 15 weeks of age when HD-like symptoms had developed, analogous to the presymptomatic and symptomatic human HD patient serum samples. Previous studies have identified a small number of potential biomarkers of HD, including the malonate ion and the branched chain amino acids leucine, isoleucine and valine. To further examine these potential biomarkers using our NMR analysis, the exact location of these biomarkers in our metabolic profiles was established by spiking purified compounds into various matrices at different concentrations. This technique enabled us to identify the NMR peaks to which these molecules contributed so that we could analyse those regions of the NMR spectrum in the various different populations of patients that were used in the TAMAHUD study.

The cross-sectional analysis of the human samples highlighted several regions of interest in the metabolic profile that contributed to being able to separate patients with symptomatic disease and controls. These were regions corresponding to unsaturated lipids, which were higher in subjects with HD than controls, and the sugar region, which was generally lower in subjects with HD than controls. Predictions of unknown samples made using models composed of these regions together with the regions corresponding to leucine, isoleucine and valine were statistically significant. It is of note, however, that this prediction was significant on a population basis, but was of insufficient accuracy to predict whether or not a single sample came from a patient with HD or a healthy control.

Analysis of the longitudinal samples from patients with HD gave generally weaker results than the cross-sectional analysis. Some models built were internally valid, but were unable to predict the status of unknown samples. Nevertheless, it is of interest that the main regions of interest were again the unsaturated lipids and sugars. In particular, one sugar peak was of much greater importance than the others in this analysis.

The results from the analysis of the transgenic mouse model of HD were similar to those from the human samples. While internally consistent models were built to distinguish the HD mice from control

mice, no useful models were found that described the progression of symptoms from younger to older mice. In contrast to the models built with the data from the human samples, the variables contributing most to the mouse models were the sugar region, with the lipids being of secondary importance. Most interestingly, however, the same individual sugar peak that was important in the longitudinal analysis of the human disease was by far the most important peak in the analysis of the mouse samples. Overall, this suggests that the transgenic mouse model of HD mirrors to some extent both the existence and progression of HD in the human population.

Integrating the data from each of the analyses into a simple model is not easy. There is some consistency with the data from the amino acid regions of the spectra, with a general decrease in levels of the branched chain amino acids in patients with HD, and a general lowering with progression of disease. Some decreases are also seen in the mouse model of HD. However, there is less consistency in the levels of the putative novel biomarkers. For example, whereas levels of the unsaturated lipids were elevated in the patients with HD in the cross-sectional study, in the longitudinal analysis the very same lipids were decreased more in the symptomatic patients than in the presymptomatic patients, back to the levels seen in the control subjects from the cross-sectional analysis. Overall, this study has given us some indications as to which types of metabolites may be useful as biomarkers of progression of HD. In particular, there is a single sugar peak (of as yet unknown molecular structure) that appears to be important in all of the models built, pulling together data from the human and transgenic mouse studies. This early stage work is clearly insufficient to be described as a biomarker for HD progression, but work will continue to try and identify this molecule and to test its suitability as a marker either for HD or for progression of HD.

Dissemination of knowledge

Overview table

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
Overall Period	***Project web-site***	***General Public***	**worldwide**		***SIBI***
05/2007	***Press release (press)***	***General public***	***Italy***		***SIBI***
18/05/2007	***Article – Finanza Mercati***	***General public***	***Italy***		***SIBI***
18/05/2007	***Article – Corriere di Siena***	***General public***	***Italy***		***SIBI***
06/07	***Article – Nova 24***	***General public***	***Italy***		***SIBI***
07/2008	***Presentation***	***Research***	**Europe**	***>100***	***SIBI***
08/2008	***Presentation***	***Research***	**Worldwide**	***>100***	***SIBI***

Meetings

- The kick-off meeting was held in Siena – IT on the May 10th-11th 2007 (Certosa di Pontignano). It was organized by SiBi, which took care of the scientific agenda and of the meeting minutes. The complete list of the participants is available in the restricted area of the TAMAHUD website.

- The 1st Annual meeting was held in Cambridge - UK on the September 18th-19th 2008. The logistic organization was done by partner 2 – CAM SIBI with the coordination of SIBI that took care of the scientific agenda and of the meeting minutes.
- The 2nd Annual Meeting was held in Siena – IT on November 13th, 2009. The logistic organization was done by partner 1 – SIBI, which took care of the scientific agenda and of the meeting minutes.
- Final TC was held on January 14th, 2011. It was organized by partner 1 – SIBI, which took care of the scientific agenda and of the meeting minutes.

All the meeting has been advertised on the TAMAHUD official website (news section) in order to give to all the participants the necessary information to attend the meeting. The complete list of the participants is available in the restricted area of the TAMAHUD website.

Press release

Press releases were done by Siena biotech to present the TAMAHUD project and the other EU co-funded projects within the FP6 (ADIT, TAMAHUD, and LIINTOP) to the general public. Several articles have been published on general journals with regional and national diffusion to publicize the TAMAHUD project as well as the other EU co-funded projects within the FP6 (ADIT, DePPICT, and LIINTOP) to the general public.

Publications

TAMAHUD consortium did not publish any paper during the 3rd reporting period.

Presentation to congress

Results obtained within the TAMAHUD project in the period from month 19 to month 30, have already been presented as per the below:

- **Gonzalez-Couto E.**
  Integrating Omics Data to Unraveling Pathologic Mechanism and Identify New Target in Huntington's disease
  ESMEC, European School of Medicinal Chemistry, Urbino, Italy, July 2008
- **Heitz F.**
  Novel therapeutics for HD: a High Throughput pathway screen approach
  13th Annual world congress 'Drug Discovery & Development of Innovative Therapeutic', Boston, USA, August 2008

TAMAHUD Web Site

The TAMAHUD web site was and is still used as internal and external information tool of the TAMAHUD project. In particular, it also offers a way to the general public to interact with the project and its partners thus fostering the dialogue in all relevant areas, independent of whether these might be social, ethical or scientific. Dissemination of research results will be made with a due amount of caution in order to avoid raising false hopes of those individuals affected by Huntington's disease and their families.
The main aspects outlined in the web site are the following:

- TAMAHUD is a project co-funded by the European Union

- TAMAHUD is a project jointly supported by public and private efforts
- Excellence of partners and soundness of their expertise
- The innovation potential of the project aiming at creating a drug discovery platform across Europe
- TAMAHUD is a project of applied research, contributing to the development of drugs for treatment of Huntington's Disease, notably a disease with a large unmet medical need
- The availability of an integrated platform of state-of-the-art technologies

Web Site Objectives

- The main communication objectives of the TAMAHUD web site include:
- Increasing visibility of TAMAHUD project
- Disseminating of acquired knowledge and innovation achieved by TAMAHUD activities, in compliance with IPR protection
- Facilitating interaction between partner scientists by providing an electronic platform for easy storage and retrieval of data and all other kinds of information (e.g. project status reports etc.)
- Increasing knowledge of the involved individual researchers
- Fostering discussion and championing new ideas from third parties which can directly contact the TAMAHUD partner consortium

Target Audience

A major distinction can be drawn between internally and externally oriented tools and services in order to meet both internal and external needs. Regarding the former, a password protected part of the web site allows the consortium partners to share confidential information (e.g. official documents such as the *Technical Annex*, the *Consortium Agreement* and progress reports) while the more general information is available to the public. The addressed target audience comprises the following:

- Universities
- Public and private institutions
- Public at large for specific tasks, researchers and technicians for jobs and fellowships
- companies interested in setting collaborations
- Health specialists such as lectures, opinion leaders, researchers, health care professionals
- Institutional 'players' in the fields of health and public funds such as ministries, universities, centers of excellence, research institutes, patient's associations, health organizations
- Institutional investors and pharmaceutical companies

Interactivity

The interactivity of the TAMAHUD website is essential and hence interactive tools have been created such as an information submission form, a message board, etc... Furthermore, specific scripts, convert submitted material via a web form to e-mail or to text file stored in a secure directory on the remote server. The requests for information or any other aspects will be evaluated and, if necessary, redirected to individuals who are more suitable to deal with them.

Exploitable knowledge and its use

No exploitable knowledge has been identified during the project duration.