



dialectica

Dorotea Rigamonti

Dialectica S.r.l.

Spin-off dell'Università degli Studi di Milano

Development of innovative
Neural Stem Cell-based Systems and Assays
for drug screening approaches
in neurodegenerative diseases.

Laboratory of Stem Cell Biology and Pharmacology of Neurodegenerative Diseases

Mechanisms
and targets
in
Huntington's
Disease

Biology
of neural stem
cells

Innovative neural stem cell lines
for disease studies and
drug screening

Predictive Cell Models
for brain pathologies

Optimized neurons
for drug discovery

Assays development in
neural stem cell lines
and derivatives

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| September 2003 | Creation of a University Spin Off: ideas and strategie |
| January 2004 | Submission of the project for consideration followed by selection by <i>Progetto Scouting</i> , Bioiniziativa - Regione Lombardia. |
| July 2004 | July 27, 2004 Founding of Dialectica s.r.l. |
| September 2004 | Evaluation process with potential investors. |
| January 2006 | Signature of the Investment agreement.
Location at Nerviano Medical Sciences. |

- **Elena Cattaneo**
- **Dorotea Rigamonti**
- **University of Milano**
- **Finlombarda Gestioni SGR (Fondo NEXT)**
- **State Street Global Investments SGR (Fondo Fondamenta)**
- **Quantica SGR (Fondo Principia)**



Dialectica has 100 m² fully equipped laboratories on the 2nd floor in building 71 at Nerviano Medical Sciences in Nerviano (MI) Italy.

Nerviano Medical Sciences (NMS) is the largest pharmaceutical R&D facility in Italy and one of the largest oncology-focused, integrated discovery and development companies in Europe.

- 1) Predictive cellular models for brain pathologies.
- 2) Optimized Neurons for drug discovery.
- 3) Cell based assays for Drug Discovery in neurodegenerative diseases.

- **European Union, STEM-HD**

“Embryonic Stem cells for therapy and exploration of mechanisms in Huntington's Disease”

EU FP6-2005-LIFESCIENCEHEALTH-6, STREP, 3 year project.
Dialectica is a partner.

- **European Union, Neuroscreen**

“The discovery of future Neuro-therapeutic Molecules”

EU FP6-2005-LIFESCIENCEHEALTH-6, STREP, 3 year project.
Dialectica is a partner.

- **Regione Lombardia, Innovazioni terapeutiche in Neurofarmacologia**

Metadistretti Regione Lombardia 2006, 2 year project.
Dialectica is a partner.

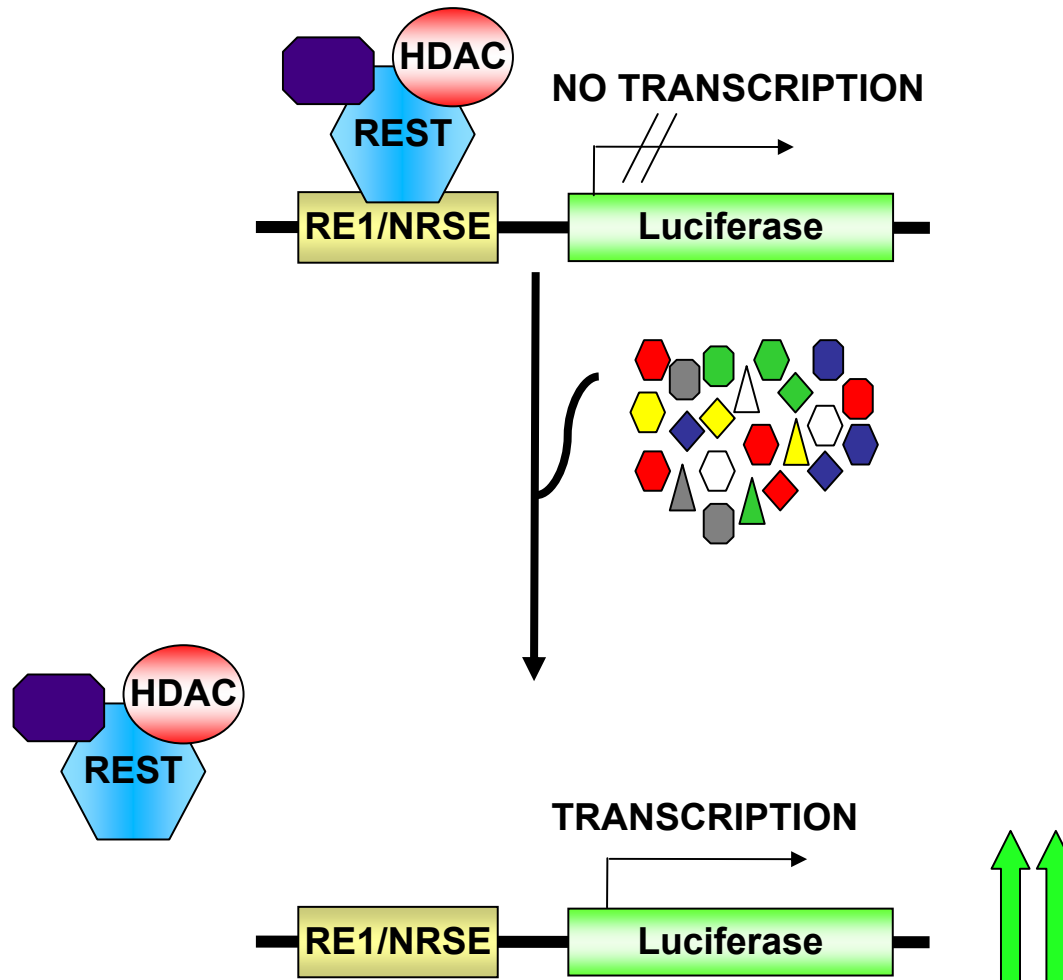
Rationale:

- 1- In Huntington's Disease and in other neurodegenerative diseases a reduced transcription of RE1/NRSE controlled neuronal genes is observed.
- 2- RE1/NRSE is a silencer element.
- 3- REST is the factor that binds to the silencer activity and activates its silencing activity.

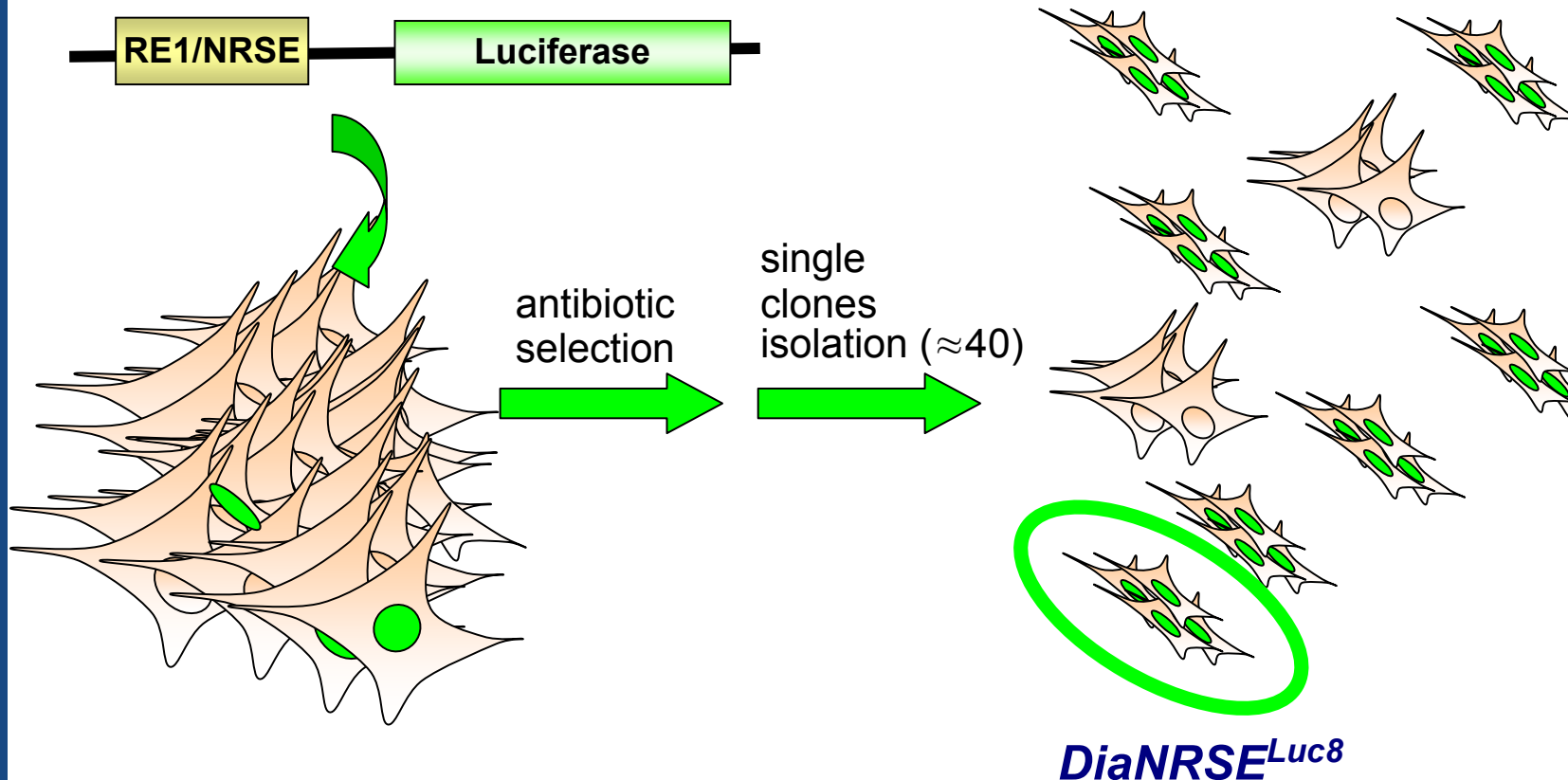
Aim:

To develop an assay allowing the identification of small molecules able to increase transcription of RE1/NRSE controlled neuronal genes.

RE1/NRSE reporter assay



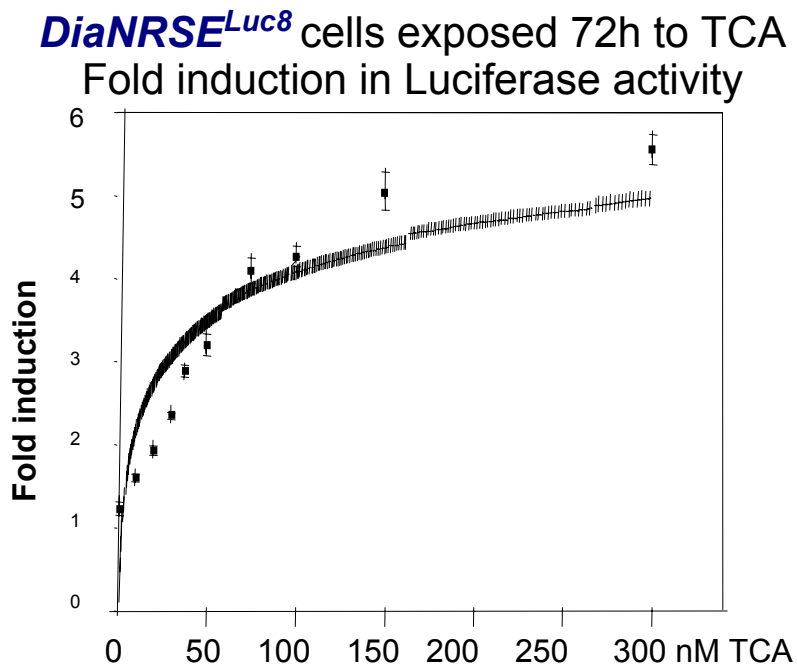
Assay development and validation: Stable clones obtainment



Chemical validation

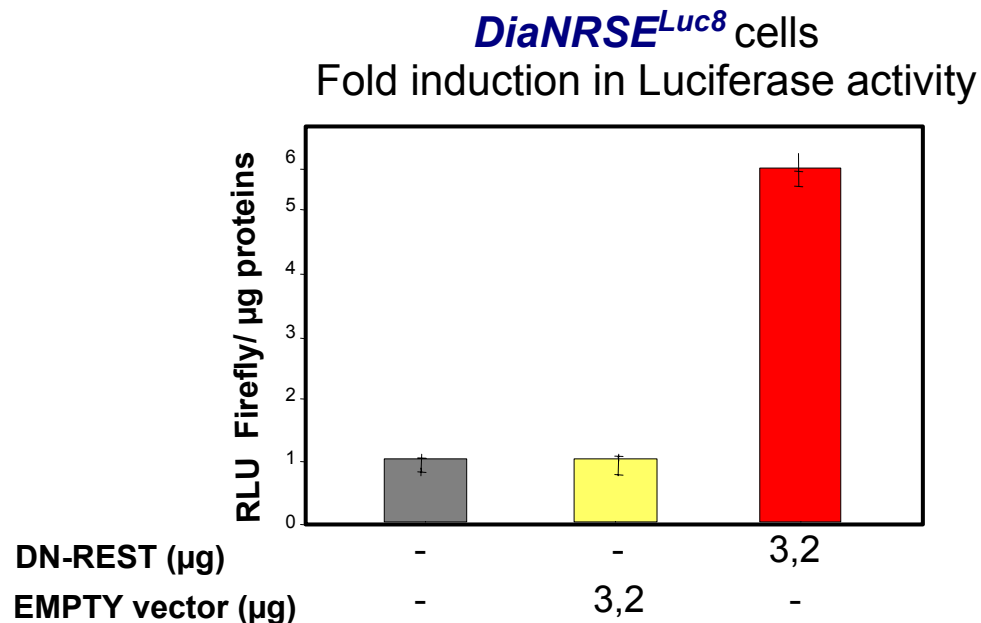
Tricostatine A (TCA), an Histone Deacetylase inhibitor and broad transcriptional activators, induces a dose-dependent increase in reporter activity.

TCA has been selected as a control compound for the screening.



Genetic validation

Infection with the Dominant Negative form of the Transcription Factor Rest (DN-REST) specifically increases reporter activity.



Three compounds active at low nanomolar concentration have been identified using this assay.

The activity has been confirmed in secondary assays

Patents:

ITALY – n. MI2002A000809 dep. 17-04-2002, EUROPE – n. 03712609.1 U.S.A – n. 511 665 dep. 18-10-2004. *Inventors:* Cattaneo E, Zuccato C (Universita' di Milano). Acquired by Dialectica from the University of Milano, January 2006.

ITALY – n. VA2006A0041 dep. 05-07-2006. *Inventors:* Cattaneo E, Rigamonti D, Kazantsev A (Dialectica srl).

The technologies developed are commercially available to identify and exploit drug targets for neuro-degenerative diseases.

Dialectica is looking for partners companies interested in co-development of innovative cellular models for drug screening or toxicological studies purposes.

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