

Scientific quote for Prof. Anna Kajaste

Project: Generation of zebrafish transgenic lines for the expression of STING F269S mutation

Project Sponsor	Università degli Studi di Pavia
Project Director	Prof. Anna Kajaste Università degli Studi di Pavia Dipartimento di Biologia e Biotechnologie via Ferrata 9 27100 Pavia CF 80007270186 P.iva 00462870189 anna.kajaste@unipv.it
Project Code	ZC_2024_CP_COLIRV_01
Quote Number	ZC_2024_CP_COLIRV_01-QT_v4.0
Date	April 8, 2025

Service and timeline

Number of genes / molecules	2 Genes
Work Packages (WP)	WP 1: Cloning of two transgenesis vectors and generation of two transgenic zebrafish lines.
Timeline	28-32 weeks

Compounds should be shipped to **ZeClinics** laboratory at:
ZeClinics - Almirall R&D. Carrer de Laureà Miró, 408-410;
08980 Sant Feliu de Llobregat, Barcelona, SPAIN

Description of the study

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WP 1: Cloning of two transgenesis vectors and generation of two transgenic zebrafish lines.

ZeClinics proposes to clone the transgene of interest in a transgenesis vector to generate two transgenic zebrafish lines using the Tol2 transposase system. In the resulting lines, the expression of the STING Wt or the STING F269S fused to GFP will be controlled by a ubiquitous promoter. Unless otherwise specified by the sponsor of the study, a fluorescent transgenesis marker will be included to facilitate the screening process.	
Experimental phase	– Design and cloning of transgenesis vector – Injection of plasmid and Tol2 into one-cell stage embryos – Screening for fluorescent reporter expression in F0 larvae – Screening of F0 and identification of a founder fish – Breeding of founder fish and delivery of F1 embryos – Animal housing and care of fish lines (4 months - 1 tank)
Genes of interest	STING Wild Type and STING F269S
Promoter	Ubb
Transgenesis marker	cry:RFP
Genetic background	Wild type
Founder Screening	2x Rounds of Founder Screening: A maximum of 40 fish that reached sexual maturity will be used for founder screening. To guarantee that enough fish are screened, Zeclinics will perform up to 3 injections and grow 60 larvae/ injection.
Deliverables	– Plasmid sequence – Pictures showing transgene’s expression – F1 transgenic embryos <i>ZeClinics does not responsabilize if the expression pattern of the chosen construct is not as expected.</i>
Service Conditions	In case the insert is lethal or leads to infertility, ZeClinics will inform the Sponsor and discontinue the project. In case of delivery of F1 and F2 embryos from a transgenesis service, it is possible that not all embryos supplied will be transgenic positive due to differences in germline transmission rates. ZeClinics recommends that embryos are always screened upon receipt and that fluorescent embryos are selected for line propagation. A 2.8 kb insert size has been assumed for the insert to be cloned in each transgenesis vector, used for the generation of the transgenic line. If the Insert is larger, prices might differ.

Important information

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Service Conditions	All the assays include material, consumables, hours of technical personnel work and use of appropriate equipment, unless otherwise specified. All assays will be conducted based on “Description of the studies” in this proposal. Changes in protocol will only be made with the previous client’s consent in writing. If any additional charge is required, a proposal amendment will be issued. Each Work Package (WP) has defined readout and deliverables; any additional analysis/readout will be quoted and invoiced in a new project.
Compound requirements	Compounds are dissolved in DMSO/E3 medium unless otherwise specified by the sponsor of the study. It is required to disclose the use of other solvents prior to signing the study. Other solvents that may cause toxicity in zebrafish are not included in this quotation unless specifically mentioned in the WPs.
Updates	Online communication upon completion of each Work Package, unless otherwise specified.
Scientific Report	Including scoring and statistical significance at project completion. All the protocolary details that are considered ZeClinics’ know-how carried out during the contracted service will not be included in the final report delivered at the end of this study.
Zebrafish lines	The company will perform up to 3 injections for the generation of a stable lines produced in our facilities. In case of a generation of a stable line, the duration of the project may be longer than specified in this quote, as genetic manipulation may cause alterations in development of the fish. In case of delivery of F1 embryos from a Knock-out service, it is possible to find multiple mutations in F1 embryos. If deletion bands of different size are observed during the genotyping of adult F1, ZeClinics recommends to sequence the different mutations in order to select only one KO allele for the propagation of an isogenic line.
Line maintenance	In case of generation of a stable zebrafish line, a back up line will be kept at ZeClinics fish facilities for up to two months after the end of the project. After that period a maintenance fee will be charged to the sponsor. In case of shipment of zebrafish lines beyond F1 generation, a backup of the line will be maintained for 3 months. Longer periods than 3 months will be charged to the sponsor.
Shipment	Shipment of samples, lines or any other material is not included in this quote, and will be invoiced separately.

Prices

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Service	N° of units	Duration	Price*
WP 1	2	28-32 weeks	14,480.00 €
SCIENTIFIC REPORT			INCLUDED
TOTAL			14,480.00 €

*Exact deadlines will be set within the following 15 natural days after signature and may be subject to holiday periods. Project starts after arrival of materials. 30% of time might be added because experimental deviations or delays caused by third-party providers. In case of exceeding the estimate duration time of the project due to non-response on the part of the Sponsor, this extended time will be subtracted from the estimated total duration.

TOTAL	14,480.00 €
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*VAT and shipment not included

Quote Acceptation

Name

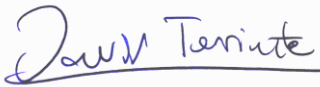
Anna Kajaste-Rudnitski

Date

08/07/2025



Signature



Javier Terriente, PhD
CCO of ZeClinics

Payment conditions

With the signing of this quote you accept the following terms of INVOICING and PAYMENT: 40% of the amount will be invoiced with the signature of this quote at the beginning of the study; 30% in the middle of the project and 30% of the amount after delivery of the final draft report/s. The payments of the invoices shall be made within thirty (30) days.

This quote is valid for 2 months from its release. In case of acceptance of it, you must send a copy by post properly signed to ZeClinics S.L., Almirall R&D. Carrer de Laureà Miró, 408-410 Zip Code: 08980 or electronically signed .pdf copy to send by email to commercial@zeclinics.com.

New experiments, studies or analytics derived from experimental guidelines and not included in this estimate, will be billed separately. In these cases, updated rates will be applied at the time of establishing new actions. The final report to the customer includes a brief description of the obtained results, raw data of each experiment performed and simple informative graphics. Statistical analysis and text detailed are not included.

Service Agreement

Terms and Conditions 1/4

This Service Agreement (the "**Agreement**") is made by and between ZeClinics SL, a duly registered company with VAT identification number ESB66058496 and principal place of business at Carrer de Laureà Miró, 408, 410, 08980 Sant Feliu de Llobregat, Barcelona, Spain (hereinafter, "**ZECLINICS**") and the Study Sponsor, referred to the Sponsor of the Study or his/her representative, if he/she is the signatory of the quote (hereinafter, the "**SPONSOR**"). **ZECLINICS** and **SPONSOR** are hereinafter collectively referred to as the "**Parties**", and individually as the "**Party**".

Whereas

- I. **ZECLINICS** is a CRO offering an outsourcing solutions using zebrafish.
- II. **SPONSOR** is the client, interested in a Services agreement in the field of life science, safety and/or efficacy assays in zebrafish (hereinafter referred to as the "**Services**").

Now therefore, in consideration of the mutual promises, covenants and conditions set forth herein, the Parties agree as follows:

1 Definitions

- 1.1 "**Agreement**" shall mean this contract research agreement.
- 1.2 "**Confidential Information**" shall mean (a) any and all information which is disclosed between the Parties either orally, electronically, visually, or in a document or other tangible form and which is by nature confidential or is identified as confidential by the Parties, related to their own business or activities; (b) experimental data, know-how, reports and any other information obtained, made or developed by the Parties in connection with the Services; and (c) its Results.
- 1.3 "**IP Rights**" shall mean all industrial and/or intellectual property rights worldwide, including without limitation any and all patents, applications for patents, continuations, continuations-in-part, divisional patents, utility patents, design patents, copyrights, trademarks, trade secrets, moral rights, database rights, rights of publication, and any other worldwide intangible or tangible right related to the Services.
- 1.4 "**Material**" shall mean any and all materials provided by one of the Parties to the other and used with connection to the Services.
- 1.5 "**Provider**" shall mean the Party that provides the Services, **ZECLINICS**.
- 1.6 "**Recipient**" shall mean the Party that receives the Services, **SPONSOR**.
- 1.7 "**Researcher**" shall mean any of the researchers appointed by the Parties for the provision of the Services.
- 1.8 "**Results**" shall mean the results, know-how, data, information, and/or reports obtained or developed directly in the performance of the Services and specifically related to according to the Agreement.
- 1.9 "**Experimental Graphic Output**" shall mean any graphic results obtained during the development of the project, contained in audio, video or picture.

2 Purpose of the Agreement

The purpose of this Agreement is to establish the terms and conditions under which **ZECLINICS** shall provide the Services to **SPONSOR**.

3 Consideration

- 3.1 In consideration of the services, **SPONSOR** shall pay to **ZECLINICS** by Bank Transfer (IBAN CODE: **ES81 0049 2354 1120 1466 9524**), according to the following terms: 40% of the amount will be invoiced with the signature of this quote at the beginning of the study; 30% in the middle of the project and 30% of the amount after delivery of the final draft report/s.
- 3.2 The payments of the invoices shall be made within thirty (30) days from the invoice dates, and only upon receipt of the corresponding invoices.
- 3.3 Payment will be made in €. For any other currency, a 1% of the total price will be charged in term of exchange-rate bank commissions

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- 3.3 The amounts shall be paid to the attention of ZECLINICS S.L., tax identification number B-66058496, billing address **Carrer de Laureà Miró, 408, 410** Postal Code: **08980 Sant Feliu de Llobregat, Barcelona, Spain.**

4 Transfer of Material

- 4.1 In the framework of this Agreement, the Parties may transfer Material to each other. Any such transfer shall be subject to the conditions of this Agreement.
- 4.2 **ZECLINICS** agrees to use the Material in compliance with all applicable laws and regulations.
- 4.3 **ZECLINICS** shall use the Material solely for the purposes of providing the Services and shall not transfer neither the Material nor modifications or derivatives to third parties who are not under any of the Researchers' direct supervision, without prior written approval of **SPONSOR**.
- 4.4 For the avoidance of doubt, **ZECLINICS** shall not use the Material for commercial purposes. Commercial use of the Material shall mean, including but not limited to:
- (a) Use of the Material for commercial purposes, such as a product offered for sale; commercial manufacture, distribution, or provision of services including quality control procedures; or for development of a directly related secondary product or service that can be sold; or
 - (b) Marketing by **ZECLINICS** or **ZECLINICS** licensee of a directly related secondary product developed using **SPONSOR's** Material.
- 4.5 Any Material provided by one Party to other Party under this Agreement shall remain the property of **SPONSOR**, unless otherwise agreed in writing between the incumbent Parties.
- 4.6 Any Material delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. **ZECLINICS** makes no representations and extends no warranties of any kind, either expressed or implied, of merchantability or fitness for a particular purpose, or that the use of Material will not infringe any patent, copyright, trademark, or any other proprietary right.
- 4.7 The shipment from **ZECLINICS's** to the **SPONSOR's** facility of the generated zebrafish lines, will be at expenses of the **SPONSOR** and not included in the price present in the price table. **ZECLINICS** will organize the shipment of larvae or adults according to the preference of the **SPONSOR** and **ZECLINICS** will manage all the paperwork and the preparation of the package. The day of the shipment, an invoice covering costs of delivery will be issued by **ZECLINICS** and sent to the **SPONSOR**.

5. Marketing: Customer Data And Graphic Material

- 5.1 The Provider will be entitled to identify the **SPONSOR** as a client on its website as well as in advertising pamphlets, with the sole purpose of reinforcing the reputation and prestige of **ZECLINICS** as a **CRO**.
- (a) This authorization includes, *numerus clausus*:
 - i. Mention of the **SPONSOR's** commercial name.
 - ii. Inclusion, next to the name, of the brand or distinctive image of the **SPONSOR's**.
 - (b) This authorization excludes expressly:
 - i. Any mention in regards to the context of the investigation carried out.
 - ii. Any mention of the price, special conditions or research objectives.
 - iii. Any mention to specific Recipient professionals.
 - iv. Any disclosure of confidential information or IP Rights.

The mentioned information will be located in a separate section of the web page ('PRESTIGE'). Under this title will appear the identification symbol of the **SPONSOR**, not existing any possibility of accessing other information than the image itself.

6. Recipient Publications

The Recipient shall include, in all the scientific publications derived from a work carried out by the Provider, a section of 'Materials and Methods' in which **ZECLINICS** is identified with its trade name and distinctive sign.

The Recipient may identify the content, part or parts of the investigation carried out by **ZECLINICS**.

Service Agreement

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7. Term and Termination

- 7.1. This Agreement shall be effective as of the Effective Date and shall remain valid until completion of the Services or until termination of the Services for any reason whatsoever occurs first. Nevertheless, the parties can decide to extend the term of the Agreement by mutual agreement in writing.
- 7.2. Any of the Parties shall be entitled to terminate the Agreement, by means of a prior notice in writing to the other Party within fifteen (15) days, as a consequence of any of the following causes:
- (a) In case of scientific and/or technical unviability of the Services always provided that the terminating Party does not remedy the scientific and/or technical unviability within the above 15-day term.
 - (b) In case of serious breach by the other Party of any of the obligations, terms, conditions, clauses or agreements under the present Agreement, including the Study Timeline detailed in Appendix 1, always provided that the infringing Party does not remedy such breach within the above 15-day term.
- 7.3. Upon request by the affected Party, the infringing Party under 7.2.b), shall bear all reasonable costs and damages caused to the affected Party because of termination.
- 7.4. Clauses 8, 9 and 13.3 shall survive termination.

8. IP Rights

- 8.1. Nothing in this Agreement shall be construed as an assignment or transfer of any IP Rights belonging to the Parties which are not granted pursuant to the Agreement. Therefore, the Parties undertake to respect each other's ownership of those rights at all times.
- 8.2. Any and all Results of the Services shall be the exclusive property of **SPONSOR**.

9. Confidentiality

- 9.1. Subject to this Agreement, both Parties agree to treat the Confidential Information with all cautions reasonably necessary and practicable to prevent its disclosure to persons other than those of their employees, consultants and/or contractors with a need to know and who are bound by like terms of confidentiality.
- 9.2. Each Party warrants that all such employees shall be obliged to maintain the confidentiality of the Confidential Information and to use it only in accordance with the provisions of this Agreement, and each Party shall use all reasonable endeavours to avoid and act against non-compliance by its employees.
- 9.3. The confidentiality obligations hereinabove mentioned shall not apply to any information that:
- (a) can be demonstrated to have been in the public domain as of the Effective Date of this Agreement, or legitimately comes into the public domain through no fault of the Parties;
 - (b) can be demonstrated to have been known to any of the Parties prior to execution of this Agreement and was not acquired, directly or indirectly, from the disclosing Party or from a third party under a continuing obligation of confidentiality;
 - (c) can be demonstrated to have been rightfully received by the recipient of the information after disclosure under this Agreement from a third party who did not require same to hold it in confidence or limit its use, and who did not acquire it, directly or indirectly, from the disclosing Party under a continuing obligation of confidentiality;
 - (d) can be demonstrated to have been independently developed by personnel of any of the Parties who had no substantive knowledge of any information provided by the disclosing Party; or
 - (e) is required to be disclosed pursuant to law or court order, provided that the recipient of the information provides prior notice to the disclosing Party and provides sufficient time to the disclosing Party to assert any exclusions or privileges that may be available by law.

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- 9.4 The obligations assumed under this clause shall remain in full force and effect not only during the term of this Agreement, but also for as long as the Confidential Information is secret and confidential and at least for a minimum period of five (5) years after termination.

10. Liability

- 10.1. Each Party shall indemnify and hold the other Parties (including its respective officers, directors, employees, agents and students) harmless from and against any and all suits, claims, demands, costs, damages, expenses, losses or injuries to persons or property caused by the breach of this Agreement, wilful or negligent act of the indemnifying Party and its officers, directors, employees, students and agents during the performance of any tasks arising out of this Agreement.
- 10.2. In no event will any Party be liable to the other Party for indirect damages regardless whether arising under contract, tort, or based upon strict liability or other theory of law or equity arising from the provision of the Services.

11. Force Majeure

No Party shall be considered to be in breach of this Agreement if such breach is caused by Force Majeure. Each Party will notify the other Parties of any Force Majeure as soon as possible. If the consequences of Force Majeure for the provision of the Services are not overcome within six (6) weeks after such notification, any of the Parties shall be entitled to terminate the Agreement.

12. Warranties

- 12.1. With regard of any information supplied by one Party to other Party under the provision of the Services, no warranty or representation of any kind is made, given or implied as to the sufficiency or fitness for purpose, nor as to the absence of any infringement of any proprietary rights of third parties.
- 12.2. Both Parties shall in all cases be entirely and solely liable for the use to which it puts such information.
- 12.3. Each Party represents and warrants that to the best of its knowledge it is under no obligation or restriction which would in any way interfere or be inconsistent with or present a conflict of interest with the obligations undertaken herein. As a consequence, either Party undertakes to keep the other Party fully harmless and indemnified from any third party claims arising from inconsistencies, interferences or conflicts of interest.

13. Miscellaneous

- 13.1. Amendments and modifications to the text of this Agreement shall be valid only if made in writing and signed by an authorized signatory of each of the Parties.
- 13.2. Should any provision of this Agreement become invalid, illegal or unenforceable, whether in whole or in part, this shall not affect the validity of the remaining provisions of this Agreement. In such a case, the Parties concerned shall be entitled to request that a valid and practicable provision be negotiated which most nearly fulfils the purpose of the original provision.
- 13.3. Neither Party will use the name, trade name, trademark or other designation of the other Parties in connection with any products, promotion, advertising, press release, or publicity without the prior written permission of the other Party.

14. Governing Law and Jurisdiction

- 14.1. This Agreement shall be governed by and construed under the laws of Spain.
- 14.2. With express waiver to any other jurisdiction that may correspond to the Parties, any dispute or controversy in relation to, in connection with or resulting from this Agreement that cannot be solved amicably between the Parties shall be submitted to the exclusive jurisdiction of the courts of the city of Barcelona.