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A BIOSCIENCE COMPANY

2022 CATALOGUE

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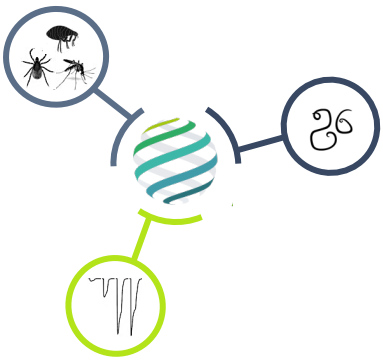
Table of content



"Every brilliant experiment, like every great work of art, starts with an act of imagination."

Jonah Lehrer

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Who are we ?

INVENesis is led by a team of dedicated scientists with decades of experience in industrial R&D and a track record of successful drug discovery in a large pharmaceutical company.

Elodie V. Rufener
Co-founder, CFO

Lucien Rufener, PhD
Co-founder, CEO

Thomas Duguet, PhD
CSO

Jacques Bouvier, PhD
Chief Advisory Board

Stéphane Wohlhauser
Laboratory technician
Assays and parasites breeding

Anouk Sarr
Laboratory technician
Molecular biology
Electrophysiology

Yves Desaules
Laboratory technician
Automated liquid handling

Gautier Pizzolon
Laboratory technician
Junior scientist

Coralie Belgrano
Laboratory technician
Junior scientist

Kevin Shoetan
Laboratory technician
Apprentice

INVENesis is also present outside Switzerland:

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France

Alexandre Vernudachi, PhD
Managing Director

Japan consulting

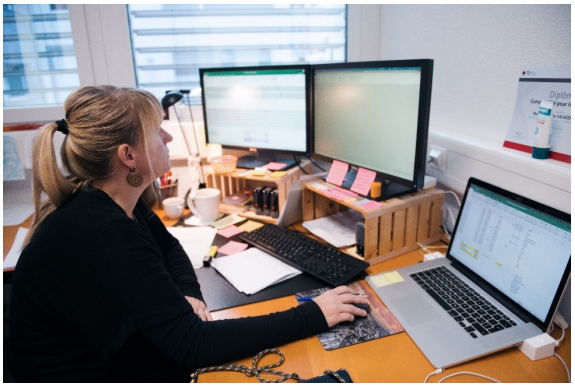
Ken Irie, PhD
External consultant

Our missions

INVENesis is a **one stop shop** to study the effect of active ingredients on individual targets, organs and whole organisms. This catalogue presents the list of validated assays for testing small molecules and natural extracts (e.g. peak correlation from HPLC extracts), many of them being compatible with **HTS campaigns and supported by automatized processes**. We propose assays on **nematodes, insects, acari, sea lice, zebrafishes** as well as **enzymatic** and **electrophysiological** assays on ***Xenopus laevis* oocytes** (functional assays on reconstituted ion-channels and transporters from invertebrates and vertebrates).

- **Organism-based assays:** their key advantage rely on the **measurement of phenotypes independently of molecular target assumptions**. We developed a whole pipeline of assays to allow high-throughput with high value assays for hit identification, lead optimization as well as resistance evaluation. Active compounds in organism-based assays have not only to act on their targets but also have to cross biological barriers, resist metabolization and reach one or more targets causing an effect at the **whole - organism level**.

- **Electrophysiology assays:** represent our second main domain of activity. The *Xenopus* oocyte expression system allows to express **functional ion-channels** in the membrane of individual cells and measure their **physiological function**. We measure the effect of compounds on **ligand-gated ion-channels, voltage-gated ion-channels, GPCRs** and **transporters**. Oocytes are injected with cDNA or cRNA encoding the receptor of interest using an automated injection platform (Roboinject). The effect of compounds on the heterologously expressed channels are recorded using an **automated two electrodes voltage-clamp automate** (HiClamp, Multichannelsystem). This system does not require months of cell culture: **we can inject on a weekly basis** and start measurements after 2-3 days of expression. We process automated protocols to detect **agonism, antagonism, positive** and **negative modulators** as well as **silent agonists**. Compounds can be pre-applied or co-applied with the natural agonist or applied alone. As the oocyte is moved across wells, this method is **non-destructive,** and measurements of other cells can be performed in a unique sample. We can also measure the electrophysiological response of sensory organs in mosquitoes and ticks.
- **Our confidentiality commitment:** to ensure a total confidentiality to our customers, we do anonymize their company name as well as each compounds we receive. In addition, the entire billing process is kept in house and managed directly by our CFO (Elodie Valazza Rufener) allowing a fast and reliable accounting.



INVENesis (Switzerland)

Established in St-Blaise on the Neuchâtel lake shore, INVENesis in Switzerland beneficiates from brand new state of the art laboratories with a total surface of 370m^2 (including 100m^2 of BSL2 labs). INVENesis in Switzerland is in charge of performing all ectoparasite and electrophysiology based assays. The company's headquarters are located there.

INVENesis France

Located on the INRAE research center in Nouzilly (France), our sister company INVENesis France takes advantage of both a facilitated access to endoparasitic species of veterinary importance and of years of collaboration with top level scientists in parasitology. INVENesis France is in charge of performing all our endoparasite-based assays and our french customers can benefit from the "Crédit impôt recherche", a fiscal-based cost reduction initiative.

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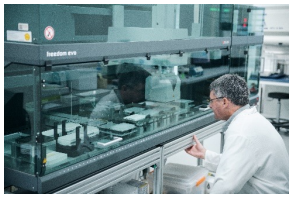
Our labs

BSL1 lab space:

- Bacteriology
- Molecular biology
- Electrophysiology



Automatized pipetting platform


BSL2 lab space:

- Parasite breeding
- Assay recording
- R&D



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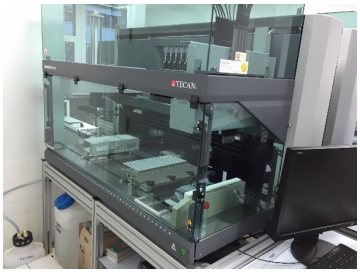
Main technical equipments

Automatized liquid handling

Chemical storage cabinets

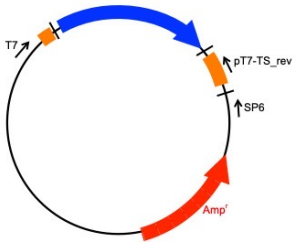


TECAN 8 tips
(serial dilutions)

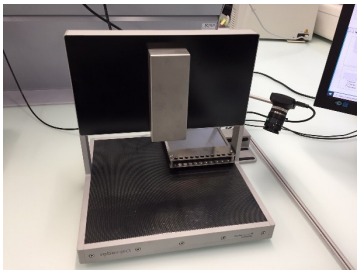
TECAN 96 / 384 tips
(test plate prep)

Liconic - KIWI
(hit picking and compound storage)

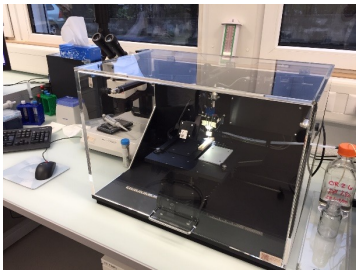
Electrophysiology platform



Molecular biology
(DNA / RNA / protein equipment)



Roboinject
(X. laevis oocyte cRNA injection)

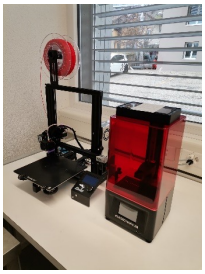


HiClamp
(X. laevis oocyte TEVC)

Other technical platforms

PCR / qPCR
(Roche Lightcycler® 480 II)

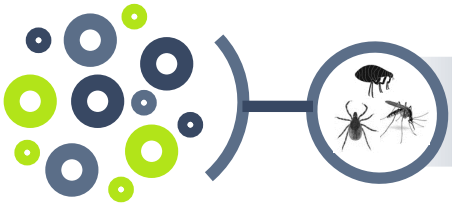
Microscopy
(Leica DMI6000B)



3D-printing
(R&D)

- Incubators
- Centrifuges
- Safety cabinets
- Fume hoods
- -80°C freezers

BSL1 / BSL2
(standard equipment)



Ectoparasites / vectors

Oral

- **INV-T-009**: Flea oral
- **INV-T-012**: Blowfly adult oral
- **INV-T-020**: Tick adult oral NEW

Tarsal

- **INV-T-010**: Flea tarsal
- **INV-T-017**: Tick egg-to-larvae tarsal
- **INV-T-018**: Tick nymph tarsal
- **INV-T-019**: Tick adult tarsal
- **INV-T-033**: Mosquito adult contact
- **INV-T-039**: Whitefly adult contact NEW
- **INV-T-042**: Tick larvae tarsal NEW

Repellency

- **INV-T-022**: Tick larvae repellent
- **INV-T-021**: Tick nymph vertical repellent
- **INV-T-029**: Tick adult vertical repellent
- **INV-T-025**: Mosquito adult repellent (1 warm body)
- **INV-T-030**: Mosquito adult repellent (2 warm bodies)
- **INV-T-040**: Whitefly adult repellent NEW
- **INV-T-043**: Flea adult repellent NEW

Development

- **INV-T-011**: Blowfly egg-to-L3 development
- **INV-T-027**: Flea development

Immersion

- **INV-T-016**: Sea lice copepodites immersion
- **INV-T-028**: Tick adult immersion

Sterilization

- **INV-T-032**: Dust acarian mixed population
- **INV-T-035**: Flea oral development NEW

Endoparasites

Development

- **INV-T-005**: Gastrointestinal nematodes larval development (egg to L_3)

Immersion

- **INV-T-004**: *Fasciola hepatica* adult immersion
- **INV-T-006**: Gastrointestinal nematodes L_3 immersion
- **INV-T-031**: Migration trap assay (MTA) NEW
- **INV-T-041**: Gastrointestinal nematodes adult immersion NEW

Model organisms

Development

- **INV-T-001**: *Caenorhabditis elegans* development (egg to L_4)
- **INV-T-003**: Zebrafish development (egg to 72h embryo)

Electrophysiology

Xenopus oocyte

- **INV-T-502**: *Xenopus* oocytes, agonist protocol
- **INV-T-503**: *Xenopus* oocytes, antagonist protocol
- **INV-T-504**: *Xenopus* oocytes, PAM or NAM protocol
- **INV-T-505**: *Xenopus* oocytes, 123 protocol
- **INV-T-506**: *Xenopus* oocytes, IVC protocol
- **INV-T-507**: *Xenopus* oocytes, custom protocol

Enzymatic assays

Enzymes

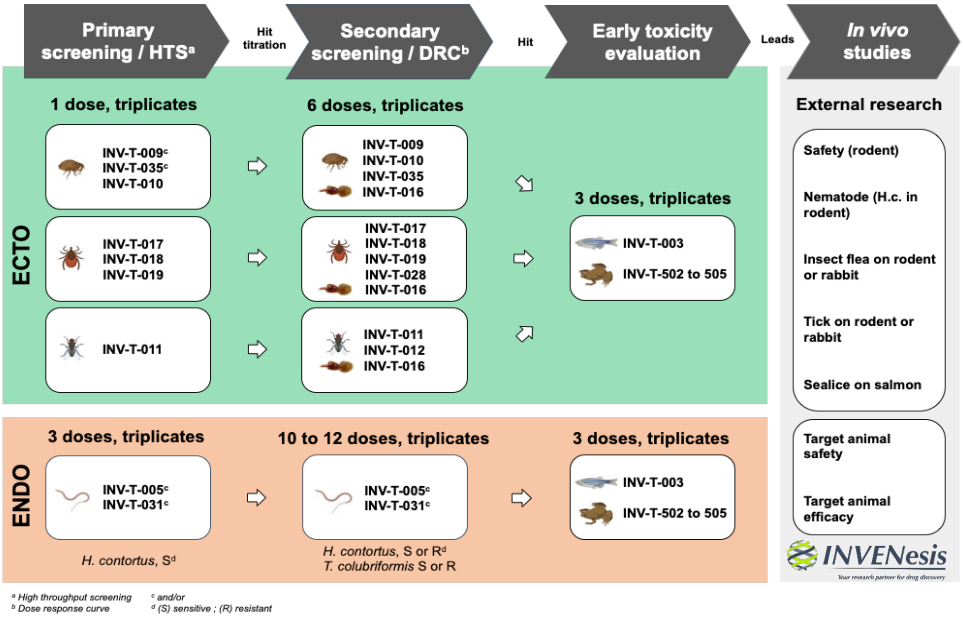
- **INV-T-023**: Microtubulin polymerization
- **INV-T-034**: Acetylcholine esterase inhibition

Assay throughput

Assay	Test ID	Rep/DTP	Compound (mg)	Max datapoint / year	Assay throughput	Price discount (HTS)
Flea oral *	INV-T-009	3	< 2	32'000	+++	++++
Blowfly adult oral	INV-T-012	3	< 2	Project-based	+	++
Tick adult oral	INV-T-020	2	< 15	160	+	+
Flea tarsal *	INV-T-010	3	< 2	32'000	+++	++++
Tick egg-to-larvae tarsal	INV-T-017	3	< 2	> 100'000	++++	++++
Tick larvae tarsal	INV-T-042	3	< 2	> 100'000	++++	++++
Tick nymph tarsal	INV-T-018	3	< 2	32'000	+++	++
Tick adult tarsal	INV-T-019	3	< 2	32'000	+++	+
Mosquito adult contact	INV-T-033	3	< 15	Project-based	+	+
Whitefly adult contact	INV-T-039	3	< 15	Project-based	+	+
Tick larvae repellent	INV-T-022	3	< 2	Project-based	++	++
Tick nymph vertical repellent	INV-T-021	3	< 15	Project-based	+	+
Tick adult vertical repellent	INV-T-029	3	< 15	Project-based	+	+
Mosquito adult repellent 1 *	INV-T-025	3	< 2	Project-based	+	+
Mosquito adult repellent 2	INV-T-030	3	< 2	Project-based	+	+
Whitefly adult repellent	INV-T-040	3	< 15	Project-based	+	+
Blowfly development *	INV-T-011	3	< 2	32'000	+++	++++
Flea development	INV-T-027	3	< 2	1'000	+	++++
Sea lice copepodite immersion	INV-T-016	3	< 2	10'000	+++	+
Tick adult immersion	INV-T-028	3	< 2	10'000	+++	+
Dust acarian mixed population	INV-T-032	3	< 2	Project-based	+	++
Flea oral development	INV-T-035	3	< 15	10'000	+	+
Gastrointestinal nematodes larval development	INV-T-005	3	< 2	100'000	++++	++
F. hepatica adult immersion	INV-T-004	3	< 15	500	+	++
Gastrointestinal nematodes L_3 immersion	INV-T-006	3	< 2	On request	++++	++
Gastrointestinal nematodes adult immersion	INV-T-041	3	< 15	On request	+	+
Migration trap assay	INV-T-031	3	< 2	100'000	++	++
C. elegans development *	INV-T-001	3	< 2	> 100'000	++++	+++
Zebrafish development	INV-T-003	3	< 2	10'000	++	++
Xenopus oocytes, agonist *	INV-T-502	3	< 1	5'000	++	++
Xenopus oocytes, antagonist *	INV-T-503	3	< 1	5'000	++	++
Xenopus oocytes, PAM/NAM *	INV-T-504	3	< 1	5'000	++	++
Xenopus oocytes, 123 *	INV-T-505	3	< 1	5'000	++	++
Xenopus oocytes, IVC *	INV-T-506	3	< 1	5'000	++	++
Xenopus oocytes, custom *	INV-T-507	3	< 1	5'000	++	++
Microtubulin polymerization	INV-T-023	2	< 1	> 50'000	+++	+
Acetylcholine esterase inhibition	INV-T-034	2	< 1	> 50'000	+++	+

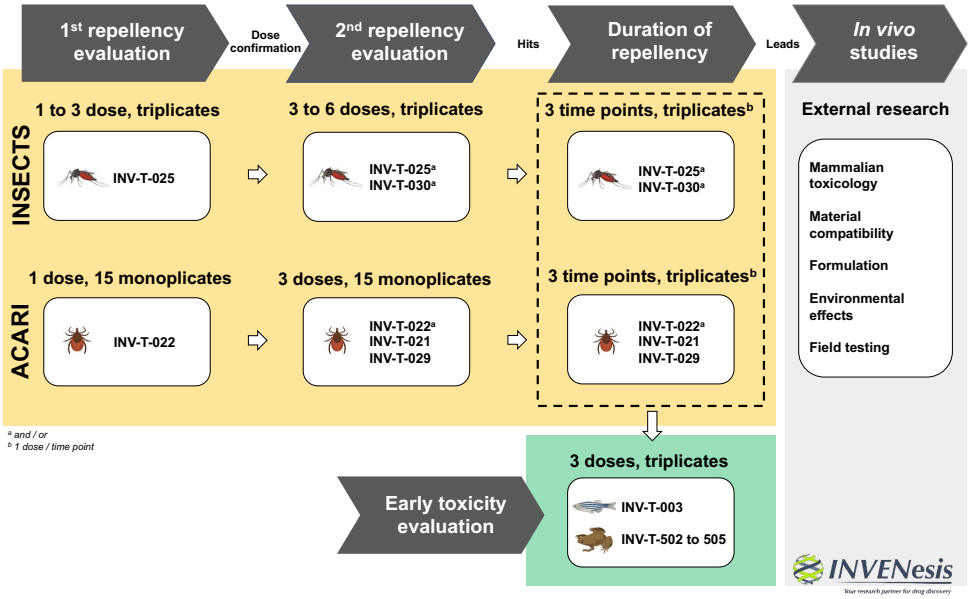
** Assays performed on a weekly basis*

Animal Health screening cascade proposal



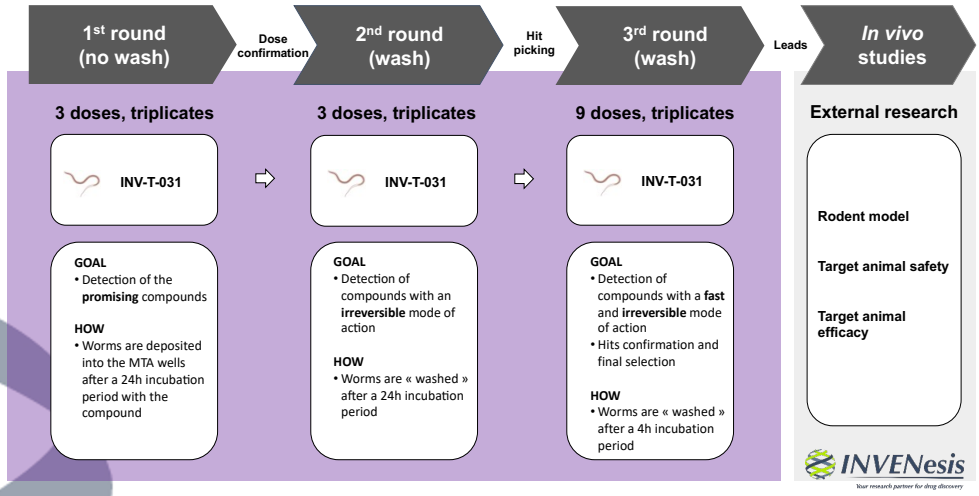
[a] High throughput screening
[b] Dose response curve
[c] and/or
[d] (S) sensitive ; (R) resistant

Repellency assays - cascade proposal

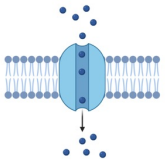


[a] and / or
[b] 1 dose / time point

Motility Trap Assay - flowchart

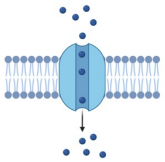


List of available or under cloning* receptors



Category	Species	Ligand
Arthropods	*Tetranychus urticae*	Acetylcholine*
		GABA*
		Glutamate*
		Glycine*
	Varroa destructor	Acetylcholine*
		Glutamate*
	Ctenocephalides felis	Acetylcholine*
		GABA
		Glutamate
	Lepeophtheirus salmonis	Acetylcholine
		GABA
		Glutamate
	Rhipicephalus microplus	Acetylcholine*
		GABA
		Glutamate
	Aedes aegypti	Acetylcholine
		Octopamine
		Tyramine
		Histamine
		Voltage-gated channel
	Drosophila melanogaster	GABA
		Phenylacetaldehyde
		Propionic acid
	Apis melifera	Acetylcholine*

List of available or under cloning* receptors



Category	Species	Ligand
Nematodes	***Ascaris caninum***	GABA
	Dirofilaria immitis	Acetylcholine*
		Amine*
		Ca^{2+} and Voltage-gated
		GABA
		Glutamate
		Glycine*
		Serotonine
	Haemonchus contortus	Acetylcholine
		Betaine
		GABA
	Caenorhabditis elegans	Betaine
		Ca^{2+} and Voltage-gated
Vertebrates	***Canis lupus lupus***	Acetylcholine*
		Ca^{2+} and Voltage-gated
		GABA
		Glycine*
		Na^{+} and Voltage-gated*
		Serotonin*
	Gallus gallus	Acetylcholine
	Homo sapiens sapiens	Acetylcholine
	Mus musculus	Acetylcholine

Contacts

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Science EXCHANGE

www.invenesis.com

References

The following references summarizes the contribution of INVENesis in academic and / or industrial research:

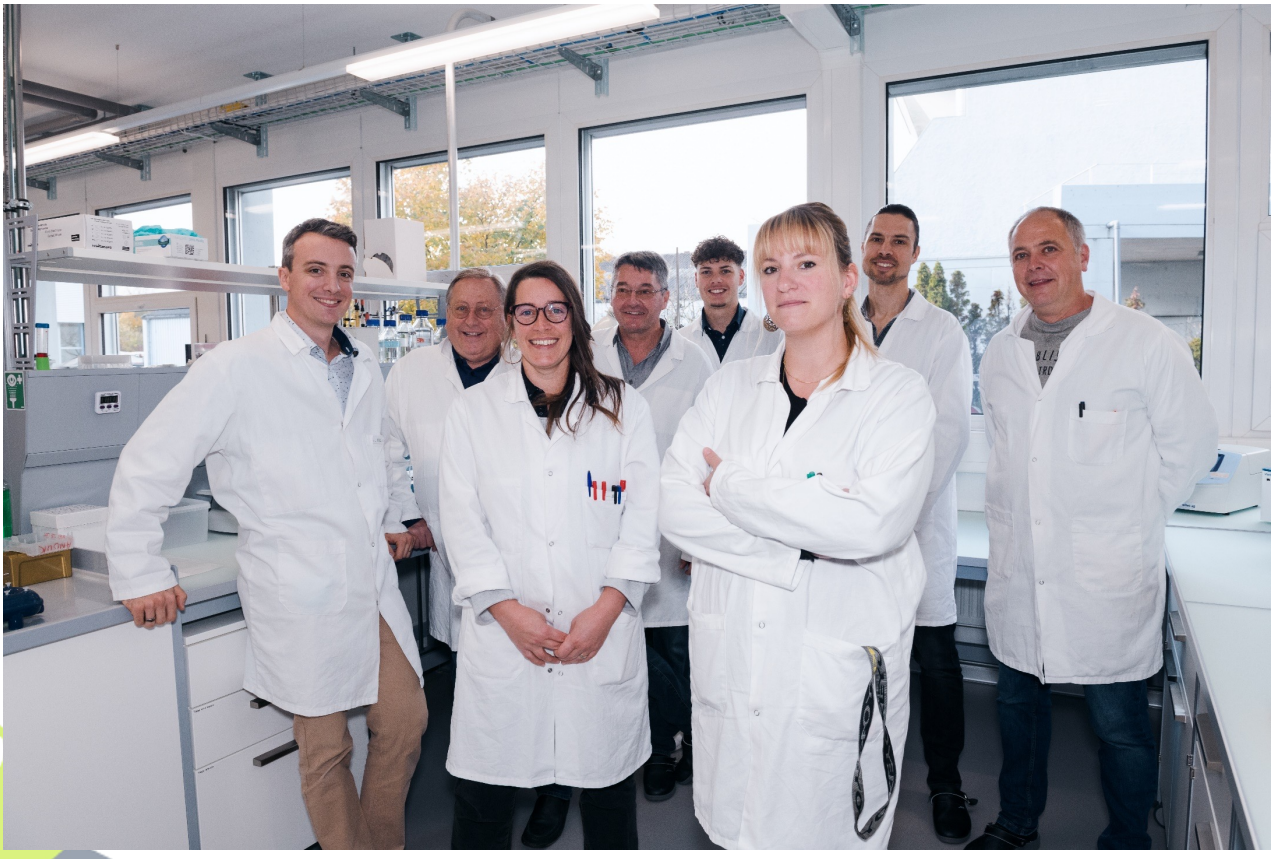
- Nicotinic acetylcholine receptors: *Ex-vivo* expression of functional, non-hybrid, heteropentameric receptors from a marine arthropod, *Lepeophtheirus salmonis*. Rufener L, Kaur K, Sarr A, Aaen SM, Horsberg TE. PLoS Pathog. 2020 Jul 27;16(7):e1008715.

- An electrophysiological characterization of naturally occurring tobacco alkaloids and their action on human α4β2 and α7 nicotinic acetylcholine receptors. Alijevic O, McHugh D, Rufener L, Mazurov A, Hoeng J, Peitsch M. Phytochemistry. 2020 Feb;170:112187.

- Antiparasitic properties of leaf extracts derived from selected *Nicotiana* species and *Nicotiana tabacum* varieties. Schorderet Weber S, Kaminski KP, Perret JL, Leroy P, Mazurov A, Peitsch MC, Ivanov NV, Hoeng J. Food Chem. Toxicol. 2019 Oct;132:110660.

- High level efficacy of lufenuron against sea lice (*Lepeophtheirus salmonis*) linked to rapid impact on moulting processes. Poley JD, Braden LM, Messmer AM, Igboeli OO, Whyte SK, Macdonald A, Rodriguez J, Gameiro M, Rufener L, Bouvier J, Wadowska DW, Koop BF, Hosking BC, Fast MD. Int. J. Parasitol. Drugs Drug Resist. 2018 Aug;8(2):174-188.

- Book chapter (in press): Discovery and development of new antifilarial drugs (*In vitro* assays). Rufener L, Vernudachi A, Kaminsky R, Duguet T.



Notes

DRUG DISCOVERY

FOR EVERYBODY

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