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各　位

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当社連結子会社(株)トランスジェニックにおける「マイクロCTを用いた髄腔内投与および脳脊髄液採取の検討」に関する学会発表について
― 微量な中枢投与と脳脊髄液の回収を可視化！ ―

当社連結子会社の株式会社トランスジェニック（代表取締役社長：高島 浩二、東京都千代田区、以下、「トランスジェニック」）は、第52回日本毒性学会学術年会において「マイクロCTを用いた髄腔内投与および脳脊髄液（CSF）採取の検討」として中枢神経系試験の技術開発成果（以下、「本成果」）を発表しましたので、お知らせいたします。本研究は、新規サービスとして展開予定の遺伝子改変動物を用いた中枢投与技術の信頼性と、安全性観察手法の確立を目的とし、次世代核酸医薬・抗体医薬の開発を支援する評価系の整備に向けたものです。

演　題：Investigation of Intrathecal Administration and Cerebrospinal Fluid Sampling Using Micro-Computed Tomography
演　者：Kazuki SATO※1, Makoto KONNO※1, Yuko DOI※1, Takuya OISHI※1, Mayumi KAWABE※1, Masahiro MOCHIZUKI※1, Masaaki KURATA※1
（※1 Trans Genic Inc.）
学　会：第52回日本毒性学会学術年会　https://www.jsot2025.jp/

【発表概要】

◆市場背景と中枢神経系評価の新たなニーズ

近年開発がすすむ核酸医薬や抗体医薬などの「バイオ医薬品」は、臓器や種によって反応が異なるため、標準的な動物モデルでは効果や副作用の正確な評価が困難です。

ICH S6ガイドライン※2では、ヒト化受容体を持つ動物モデルの使用が推奨されており、当社はその開発と応用に強みを持っています。今回の発表において、マイクロCTを用いた薬剤投与の可視化および精度の高い脳脊髄液の回収技術を確立しました。

※2　バイオ医薬品の非臨床安全性評価に関する国際的なガイドラインです。

◆試験概要及び成果（概要）※詳細は、添付発表ポスターをご参照ください。

項　目	内　容
動物	ICRマウス（雌）8週齢
投与法	脊髄くも膜下（髄腔）内投与（IT投与）
観察方法	マイクロCT（針先と薬液の位置を確認）
脳脊髄液の採取	専用針で10μL回収（血液混入リスク低減を検討中）
異常所見	軽度の行動異常（高用量群で一部確認）以外は良好

◆今後の展開

本成果は、中枢神経系を標的とする医薬品の非臨床試験において、安全かつ再現性の高い評価を実現する技術基盤となります。今後は、CSF回収法の改良（血液混入防止）、投与条件のさらなる最適化、受託試

験サービスとしての事業展開を進め、製薬企業との連携を加速させます。
　今後も、トランスジェニックは「評価できないものを評価できるようにする」を信条に、創薬の発展に資する技術開発を推進しております。今回の成果も、次世代医薬の適切な安全性評価という社会的課題への一歩と捉えております。

以上

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Investigation of Intrathecal Administration and Cerebrospinal Fluid Sampling Using Micro-Computed Tomography

○Kazuki SATO, Makoto KONNO, Yuko DOI, Takuya OISHI, Mayumi KAWABE, Masahiro MOCHIZUKI, Masaaki KURATA

Trans Genic Inc.

Introduction

Many bio-pharmaceuticals (mainly nucleic acid and antibody drugs) exhibit species- and tissue-specific biological activity, making pharmacological and on-target toxicity evaluations difficult in standard animal models. The ICH S6 guideline recommends transgenic animals expressing humanized receptors as optimal models. We are developing evaluation methods leveraging our gene modification expertise.

We examined IT administration techniques in rodents using micro-computed tomography (μCT), allowing precise visualization of the needle tip and assessment of solution leakage. Additionally, our previous CSF collection approach was labor-intensive and constrained by specialized equipment, prompting us to develop a more efficient method.

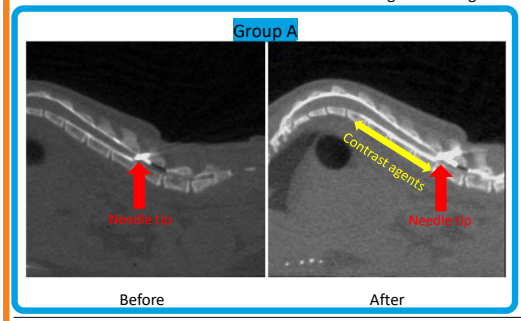
Materials and Methods

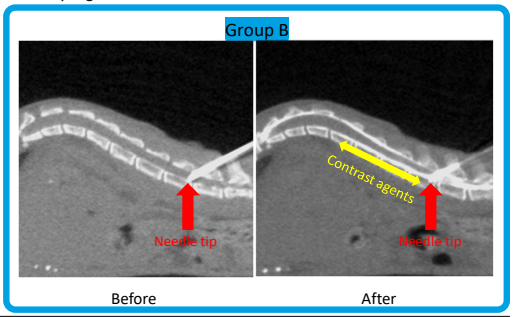
Animals : Slc:ICR［SPF］, mouse (Japan SLC, Inc.) , 8 weeks old, female, 10 animals
The conditions of the room : Temperature 20 to 26℃, Humidity 35 to 70 %
Contrast agent : Isovist injection 240 (Bayer Yakuhin Co., Ltd.)
Dosing period : Single administration (intrathecal (IT) administration)
Administration rate : 5 μL/min
Examinations : Clinical signs, body weights, the Irwin's comprehensive observational assessment, CFS sampling

Groups	Volume (μL/Head)	Number of animals	Animal No.
No treatment	-	2	1, 2
A	10	4	3～6
B	20	4	7～10

Results

1. No abnormalities were observed in the general condition or body weight of any group throughout the study period.
2. CT scans were performed on Group A and Group B before and after administration. In both groups, the contrast agent was confirmed to have been injected into the spinal cavity, and "no" leakage of the contrast agent outside the spinal cavity was observed.
3. In addition, based on Irwin's comprehensive observation evaluation, the presence and frequency of the following symptoms were observed before administration, immediately after administration, 1 hour after administration, and 24 hours after administration. At each observation point, the behavioral parameters of the animals were observed for 2 minutes in a polycarbonate box, and then reflexes and muscle tone were examined. As a result, no abnormalities were observed in the no treatment group and Group A. In Group B, abnormal spontaneous movement (walking with running) was observed in Animal No. 8, and abnormal posture (crouching) was observed in Animal No. 10.
4. After 24 hours of observation, all animals were euthanized by exsanguination, and 10 μL of cerebrospinal fluid (CSF) was collected from between the end of the skull and the first cervical vertebra using a 27G winged needle and syringe.





Symptom		Judgement (Score)	No treatment group Time after administration (h) Before	JA	1	24	A group Time after administration (h) Before	JA	1	24	B group Time after administration (h) Before	JA	1	24
No. of animals used			2	2	2	2	4	4	4	4	4	4	4	4
Posture	Body position	standing on the limbs	2	2	2	2	4	4	4	4	4	3	4	4
		crouching position	0	0	0	0	0	0	0	0	0	1	0	0
Behavior	Passivity	try to escape when picked the neck (normal)	2	2	2	2	4	4	4	4	4	4	4	4
	Aggression	none	2	2	2	2	4	4	4	4	4	4	4	4
	Restlessness	none	2	2	2	2	4	4	4	4	4	4	4	4
	Abnormal phonation	none	2	2	2	2	4	4	4	4	4	4	4	4
	Circling	none	2	2	2	2	4	4	4	4	4	4	4	4
	Rolling	none	2	2	2	2	4	4	4	4	4	4	4	4
	Stereotypy	none	2	2	2	2	4	4	4	4	4	4	4	4
	Staggering gait	none	2	2	2	2	4	4	4	4	4	4	4	4
	Abnormal gait	none	2	2	2	2	4	4	4	4	4	4	4	4
	Locomotor activity	exploratory behavior (normal)	2	2	2	2	4	4	4	4	4	3	4	4
		walk with running	0	0	0	0	0	0	0	0	0	1	0	0
	Self-Grooming	(counts/2 min/group)	2	2	2	2	4	4	4	4	4	4	4	4
	Yawn	(counts/2 min/group)	2	2	2	2	4	4	4	4	4	4	4	4
	Defecation	(counts/2 min/group)	2	2	2	2	4	4	4	4	4	4	4	4
	Urination	(counts/2 min/group)	2	2	2	2	4	4	4	4	4	4	4	4
Autonomic nervous system	Palpebral closure	normal	2	2	2	2	4	4	4	4	4	4	4	4
	Exophthalmos	none	2	2	2	2	4	4	4	4	4	4	4	4
	Salivation	none	2	2	2	2	4	4	4	4	4	4	4	4
	Lacrimation	none	2	2	2	2	4	4	4	4	4	4	4	4
	Piloerection	none	2	2	2	2	4	4	4	4	4	4	4	4
	Shivering	none	2	2	2	2	4	4	4	4	4	4	4	4
	Twitch	none	2	2	2	2	4	4	4	4	4	4	4	4
	Tremor	none	2	2	2	2	4	4	4	4	4	4	4	4
	Tonic convulsion	none	2	2	2	2	4	4	4	4	4	4	4	4
	Clonic convulsion	none	2	2	2	2	4	4	4	4	4	4	4	4
	Tachypnea	none	2	2	2	2	4	4	4	4	4	4	4	4
	Dyspnea	none	2	2	2	2	4	4	4	4	4	4	4	4
	Hypothermia	none	2	2	2	2	4	4	4	4	4	4	4	4
	Pupil	normal	2	2	2	2	4	4	4	4	4	4	4	4
	Skin color (pinna)	normal	2	2	2	2	4	4	4	4	4	4	4	4
	Diarrhea	none	2	2	2	2	4	4	4	4	4	4	4	4
Reflex and muscle tone	Startle reflex	shrink or move the pinna (normal)	2	2	2	2	4	4	4	4	4	4	4	4
	Righting reflex	return to the right position within 3 seconds (normal)	2	2	2	2	4	4	4	4	4	4	4	4
	Corneal reflex	close the eyelid (normal)	2	2	2	2	4	4	4	4	4	4	4	4
	Pinna reflex	move the pinna (normal)	2	2	2	2	4	4	4	4	4	4	4	4
	Body tone	present resistance (normal)	2	2	2	2	4	4	4	4	4	4	4	4
	Limb tone	present resistance (normal)	2	2	2	2	4	4	4	4	4	4	4	4
	Grip strength	moderate resistance (normal)	2	2	2	2	4	4	4	4	4	4	4	4
	Pain response (Tail pinch)	abnormal phonation or look back to bite (normal)	2	2	2	2	4	4	4	4	4	4	4	4

JA : Just after administration

Discussion and Conclusion

The crouching position and walking with running in the locomotion activity observed in the general observation of Group B are considered to be due to the dosage, since no abnormalities were observed in Group A. The individual with the crouching position was also observed to walk with the top of its head pressed against the floor.

In addition, although it is possible to collect CSF over time, we choose to collect it after blood removal because we cannot completely eliminate the risk of blood contamination. For this issue, we are currently exploring improvements to the collection device to reduce blood contamination.

COI Disclosure Information Kazuki Sato
In connection with this presentation, there is no COI to be disclosed with any companies.