The peptide components of Transferon Oral®, a Dialyzable Leukocyte Extract, are absorbed and biodistributed to cervical nodes after oral administration in a murine model

Fragozo A[1,2], Trejo-Martínez I[1,2], Valencia-Martínez L[1], Domínguez-Bernal K [1] Pavón L[3], Vallejo-Castillo L[1,2], and Pérez-Tapia SM[1, 2,4].

[1]Unidad de Desarrollo e Investigación en Bioterapéuticos (UDIBI), Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional, México City, México. [2]Laboratorio Nacional para Servicios Especializados de Investigación, Desarrollo e Innovación (I + D + i) para Farmoquímicos y Biotecnológicos (LANSEIDI-FarBiotec-CONACyT), México. [3]Laboratorio de Psicoinmunología, Dirección de Investigaciones en Neurociencias, Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz, México [4]Departamento de Inmunología, Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional, México.

ana.fragozo@udibi.com.mx, luis.vallejo@udi.com.mx, sperezt@ipn.mx.

INTRODUCTION

Complex drugs are composed of many active molecules with related chemical structures, requiring a different type of pharmacokinetic analysis/Mechanism of Action (MOA)[1]. Transferon Oral® is a complex mixture of less than 10 kDa peptides and is used to treat infections, allergies, and autoimmune diseases[2]. Transferon Oral® reduces the production of proinflammatory cytokines such as TNF-α and IL-6 and increases IFN-γ levels when administered orally in a mouse model of HSV-1 infection[3]. However, its MOA and pharmacokinetics are unknown. Recently, we have sequenced Transferon Oral® and evinced that is composed of more than 60 peptides with different physicochemical characteristics[4]. To shed light on the MOA and preclinical efficacy of orally-administrated peptide-derived biodrug, the biodistribution pattern must be determined.

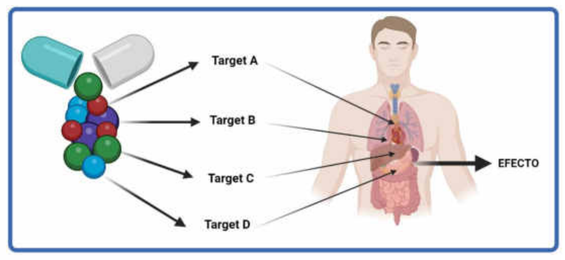
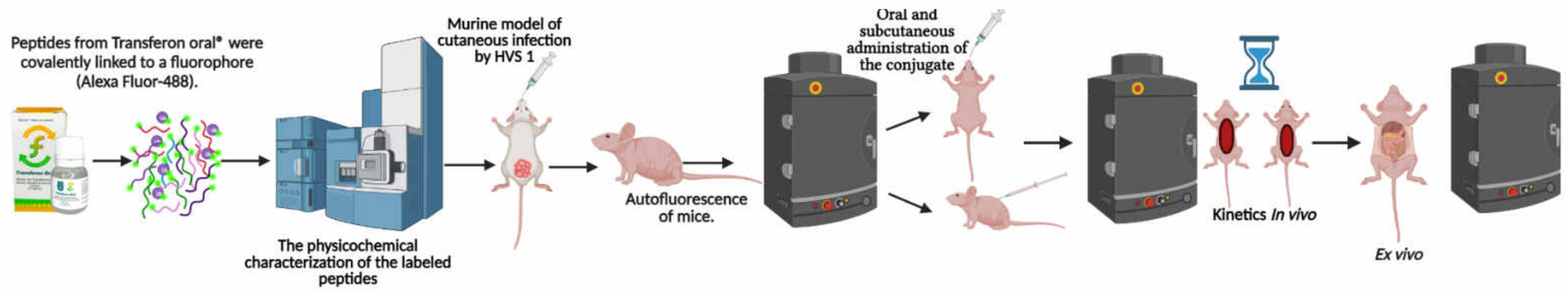


Figure. 1 Pharmacology of complex drugs

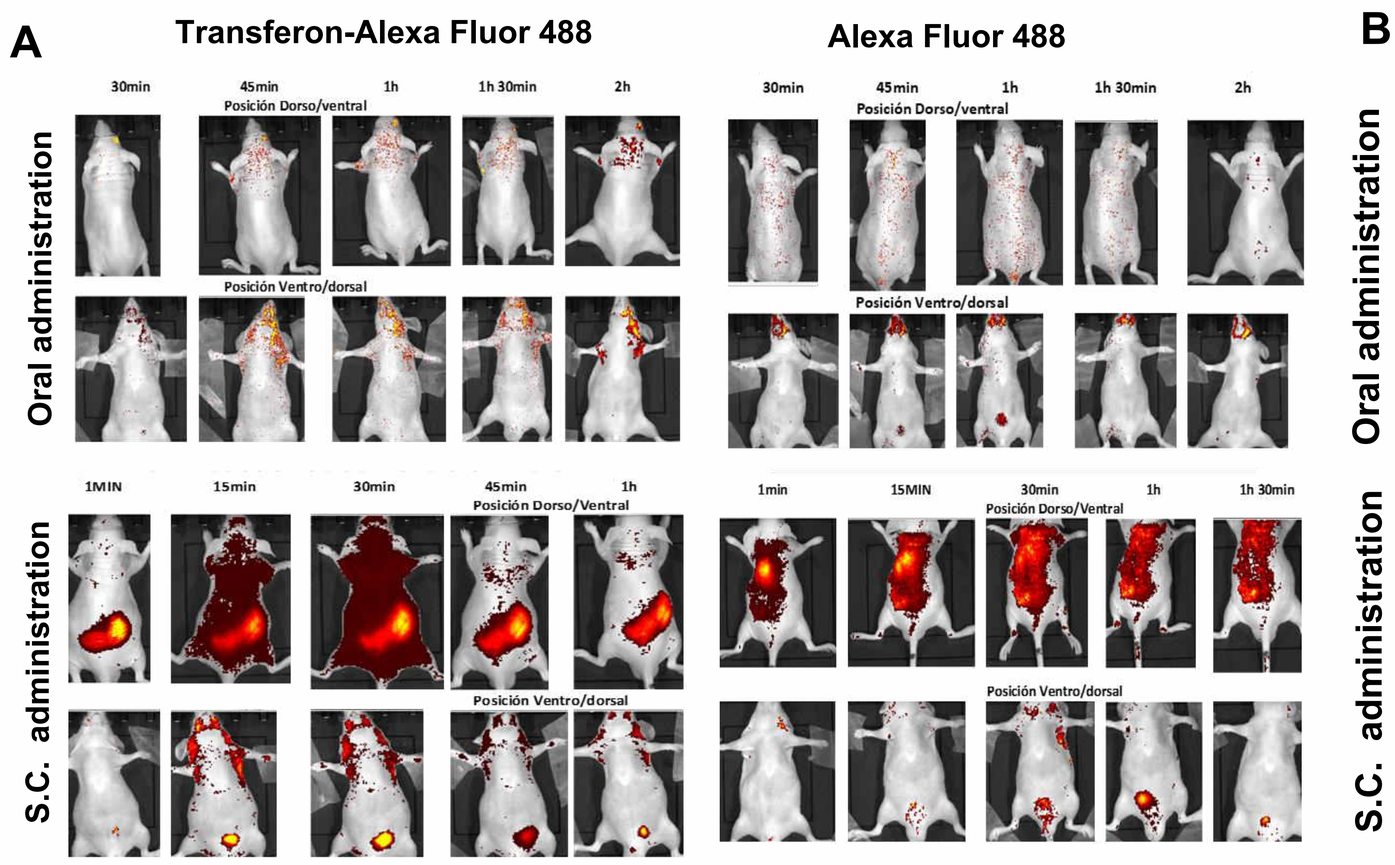
OBJECTIVE

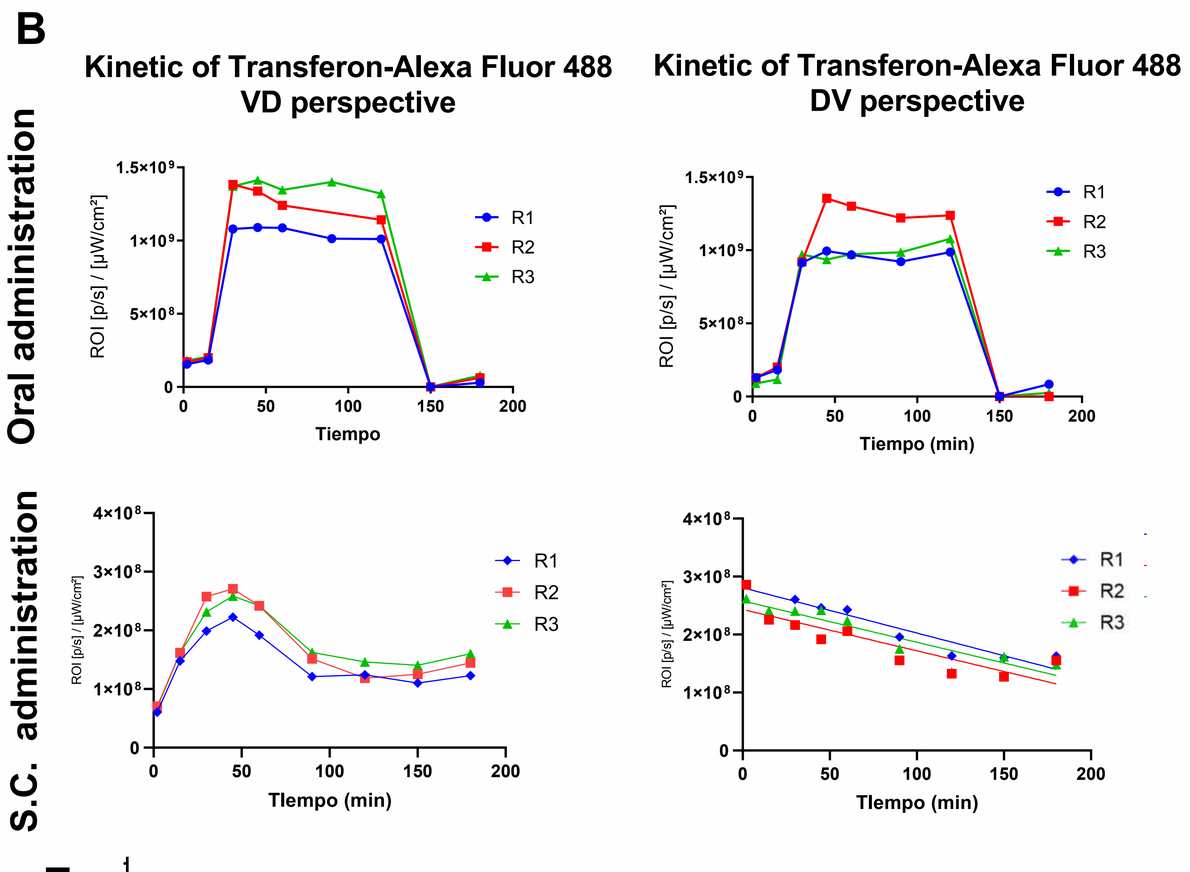
To determine the *in vivo* biodistribution pattern of the Transferon Oral® peptides using subcutaneous and intragastric administration by imagenology.

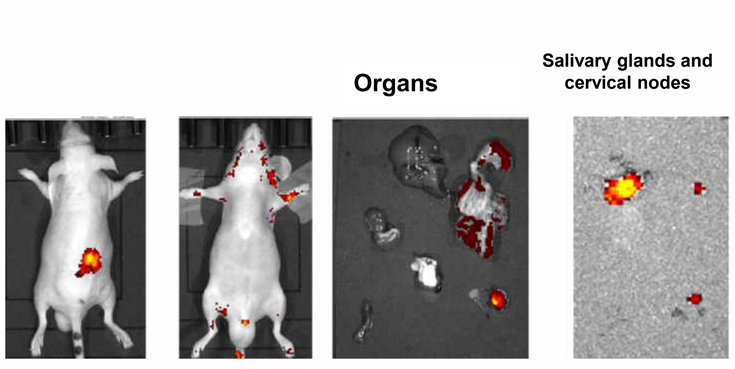
METHODS

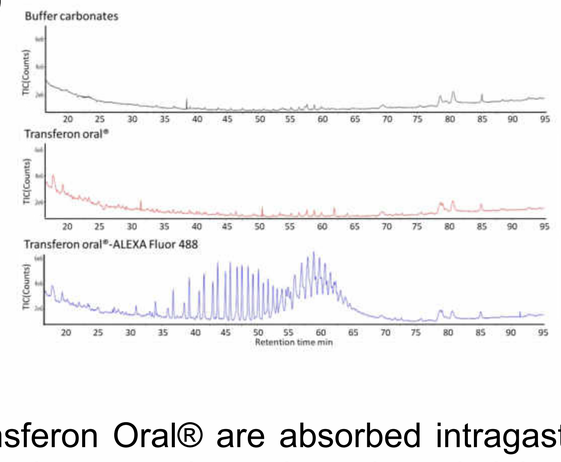


RESULTS AND DISCUSSION









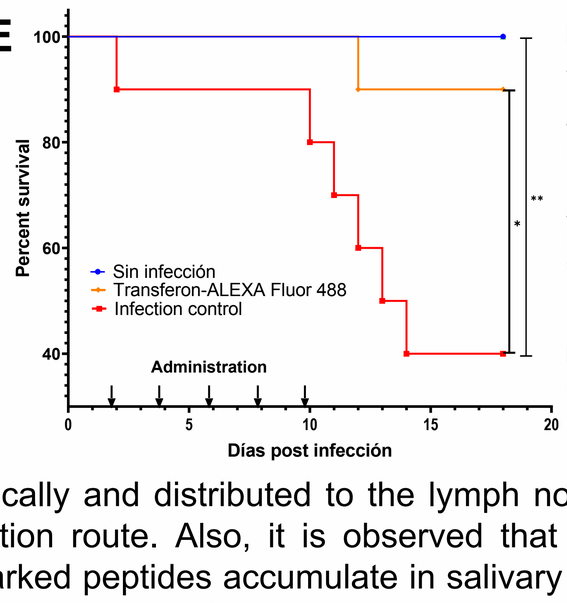


Figure. 2 Accumulation kinetics of Transferon-ALEXA Fluor 488 conjugate. A) In vivo biodistribution of Transferon Oral ® ALEXA fluor 488 conjugate by the oral and subcutaneous routes, B) Representative graph of the kinetics of Transferon Oral ® peptides conjugated with ALEXA fluor 488 by the oral and subcutaneous routes from two different perspectives: Dorso-ventral (left), Ventro-dorsal (Right), C) Ex vivo biodistribution, D) Chromatographic profile of total ion count on Transferon and ALEXA fluor 488. E) Evaluation of pepttide-conjugates functionality in a mouse model of HSV-1 skin infection.

CONCLUSION

We report for the first time that the peptides of Transferon Oral® are absorbed intragastrically and distributed to the lymph nodes. The biodistribution pattern is driven by the characteristics of the peptides, and it does not depend on the administration route. Also, it is observed that Transferon Oral® gets the blood compartment, and the peptides are filtrated in the kidneys. *Ex vivo* analysis showed that marked peptides accumulate in salivary and cervical nodes, the peripheral organs of the immune system where the immunomodulatory effects of Transferon Oral® might be triggered.

ETHICAL APPROVAL

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