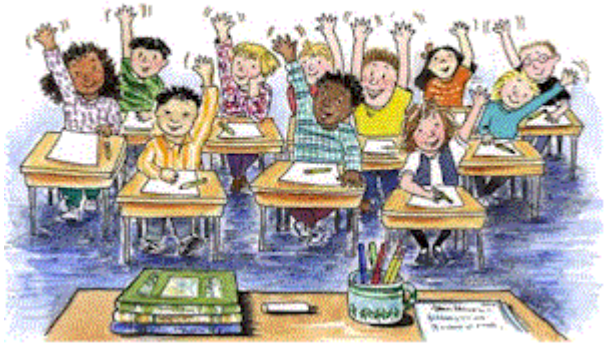
III JORNADAS DE ORIENTACIÓN PROFESIONAL

REBECA REAL FERNÁNDEZ

12 DE ABRIL DE 2013

Licenciada en biología por la Universidad de León
Promoción 1999-2004

- Oposiciones Secundaria



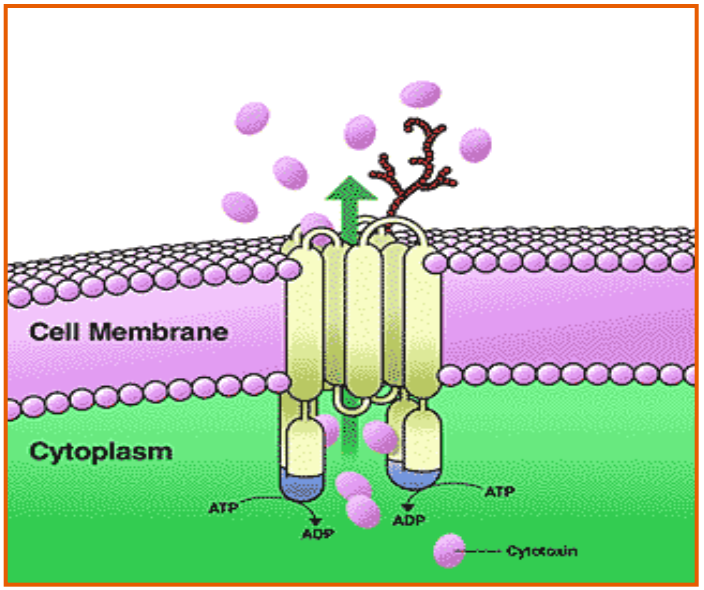
- Investigación

Beca de colaboración: Departamento de Fisiología
Curso 2004/2005

Tesina de Licenciatura Mayo 2006:

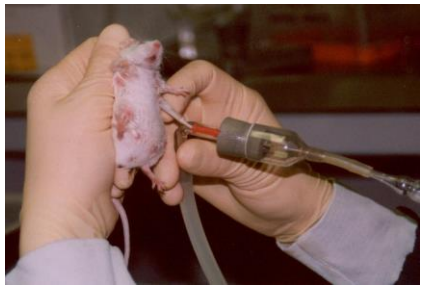
"*Papel de la proteína BCRP/ABCG2/MXR en el transporte de fármacos y papel de antioxidantes*"

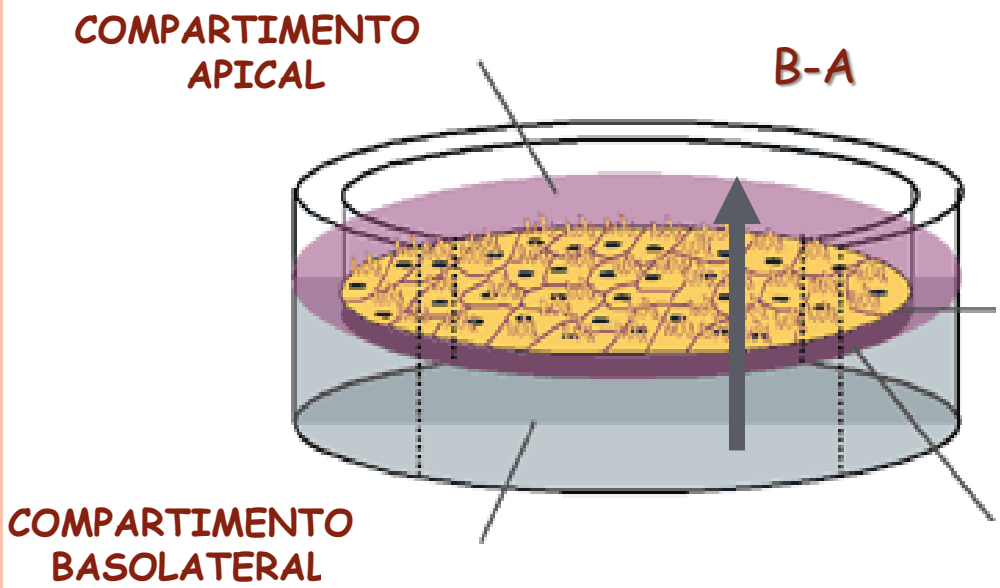
bajo la dirección de **las Dras Álvarez de Felipe y Merino Peláez**

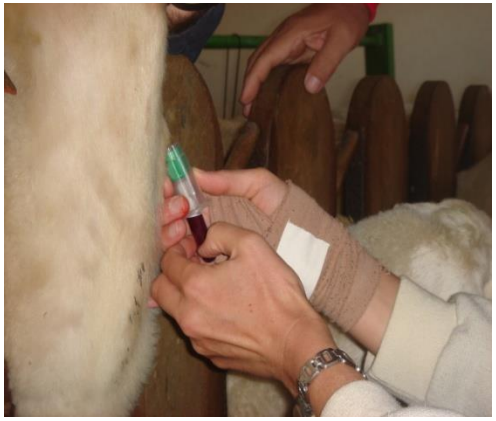


Inicio de la etapa predoctoral: beca Excma Diputación de León 2006-2009

TÉCNICAS:




COMPARTIMENTO APICAL
B-A
MONOCAPA MDCKII
FILTRO CON MICROPOROS
COMPARTIMENTO BASOLATERAL



PUBLICACIONES:

- Rebeca Real, Estefanía Egido, Miriam Pérez, Lucía González-Lobato, Borja Barrera, Julio G. Prieto, Ana I. Álvarez, Gracia Merino. ***"Involvement of Breast Cancer Resistance Protein (BCRP/ABCG2) on the secretion into the milk of danofloxacin: interaction with ivermectin"*** 2011 Aug;34(4):313-21, Journal of Veterinary Pharmacoly and Therapeutics.
- Rebeca Real, Lucía González-Lobato, Marta F. Baro, Julio G. Prieto, Ana I. Álvarez, Margarita Marqués, Gracia Merino. ***"Analysis of the effect of the bovine ABCG2 SNP Y581S on transcellular transport of veterinary drugs using new cell culture models"*** 2011 Dec;89(12):4325-38, Journal of Animal Science.

COMUNICACIONES A CONGRESOS:

In vivo interaction of danofloxacin with Breast Cancer Resistance Protein (BCRP/ABCG2)

Real R[1]; Egido E[1,2]; González-Lobato L[1,2]; Pérez M[1,2]; Prieto JG[1]; Alvarez AI[1,2]; Merino G[2].
Department of Biomedical Sciences[1], Animal Health Institute[2], University of Leon, Campus de Vegazana 24071 Leon, Spain

INTRODUCTION

Danofloxacin (DANO) is a synthetic antibacterial agent belonging to fluoroquinolone class, a family of compounds useful for the treatment of a variety of microbial infections. Some drugs included in this family are substrates of the transporter BCRP/ABCG2 (Breast Cancer Resistance Protein), (Pulido et al., (2006); Merino et al., (2006)). Recently, we have shown *in vitro* interaction of DANO with BCRP/ABCG2 (Real et al., 2008). This protein extrudes xenotoxins from enterocytes and hepatocytes as well as other epithelial cells from organs and it actively secretes drugs into the milk. DANO is actively secreted into the milk (Escudero et al., (2007)); this secretion mechanism could influence DANO effectiveness in the treatment of infections and could be potentially associated with antibiotic resistance. The purpose of this study was to determine the *in vivo* interaction of DANO with Breast Cancer Resistance Protein.

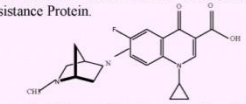


Fig. 1: Chemical structure of danofloxacin

MATERIALS AND METHODS

Pharmacokinetic studies were carried out at different times (5 to 30 minutes) and doses (5, 10, 30 and 50 mg/kg) after oral and intravenous administration, using Bcrp1 knockout mice and they were compared with wild type mice. In addition, secretion into milk was analysed in lactating females. HPLC conditions to process samples were based on Merino et al., (2006).

RESULTS AND DISCUSSION

s showed that plasma concentrations of DANO in wild type
ut mice were very similar at the doses and times studied after
travenous administration. Fig. 2 represents one example of
of experiments. However, in lactating females, milk
ion and milk/plasma ratios were significantly higher in wild
in knockout mice following intravenous administration of 10
0 minutes. (Fig. 3).

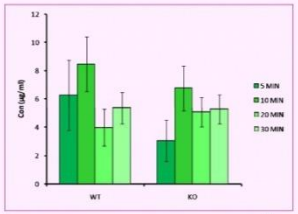


Fig. 2: Plasma concentration after DANO oral administration (50 mg/Kg) in wild type and knockout mice at different time points. Results are expressed as means and error bars indicate standard desviation (n= 4-7).

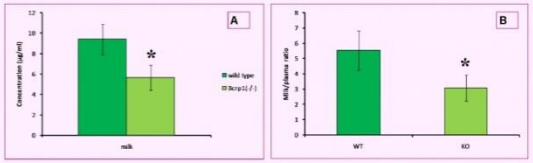


Fig. 3: Milk concentration (A) and milk/plasma ratio (B) of DANO in WT and KO lactating females. DANO was intravenously administered (10 mg/kg) and plasma and milk samples were collected after 20 minutes. Results are expressed as means and error bars indicate standard desviation. (n = 5, * p<0.01).

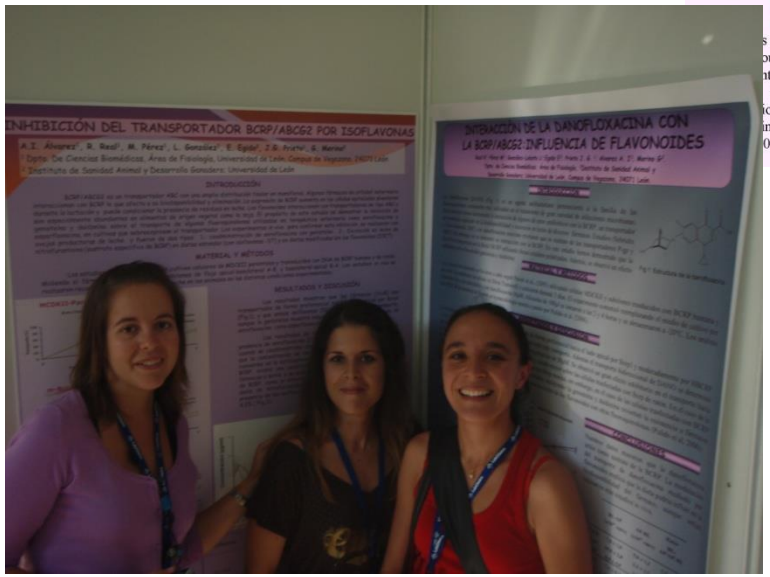
CONCLUSIONS

In this study, we have demonstrated that DANO is actively secreted into milk by the Bcrp1 transporter. Our data contribute to milk residues studies and to the understanding of resistance to antibiotics. A strategy to reduce DANO milk residues could include the inhibition of this transporter.

REFERENCES

Escudero et al. (2007) *J Vet Pharmacol Ther* **30:** 572-577. **Merino** et al. (2006) *Drug Metab Dispos* **34:** 690-695. **Pulido** et al. (2006) *J Vet Pharmacol Ther* **29(4):**279-87. **Real** et al. (2008), Communication to XXXI Congress of the Spanish Society of Biochemistry and Molecular Biology.

Supported by Ramón y Cajal grant to MG and grant AGL2006-13186 to AAI from the Ministerio de Ciencia y Tecnología, Spain; Diputación de León fellowship to RR; Junta de Castilla y León fellowship to EE and group of excellence grant GR 132 to PIG. The authors thank Dr. A.H. Schinkel who provided us Bcrp1 knockout mice.



2009 con la tesis sin terminar, y ahora que????

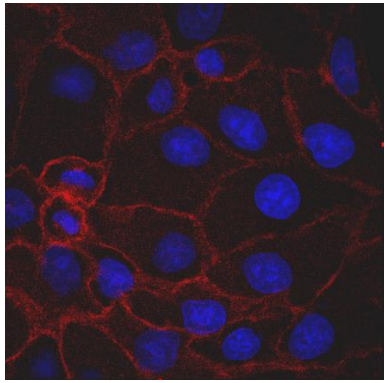
Participación en proyectos con empresas 2009-2011

Defensa Tesis Doctoral 2011

"Caracterización del transportador de membrana BCRP y sus polimorfismos en rumiantes: importancia en la aparición de residuos de fármacos en leche"

bajo la dirección de las doctoras **Merino Peláez** y **Marqués Martínez**

- Caracterización del transportador BCRP: cultivo in vitro de células MDCKII que sobreexpresan el transportador
- Estudios in vivo: ratones y ovejas
- Estudio de polimorfismos del transportador de rumiantes



Y ahora qué???

ALIVIO

ICERTIDUMBRE

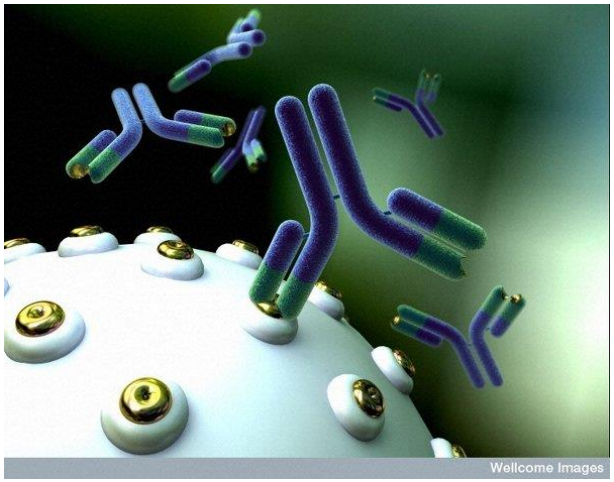
- Convocatorias públicas (postdoc)
- Salto a la empresa privada

Salto a la empresa privada : Beca ADE año 2012 en GH Genhelix

Ade
Inversiones y Servicios

The Genhelix Group
Compañía Biofarmacéutica

Producción de proteínas recombinantes mediante el cultivo in vitro de células de mamífero



- Enero 2013 contrato con la empresa

¡ÁNIMO!

¡GRACIAS!