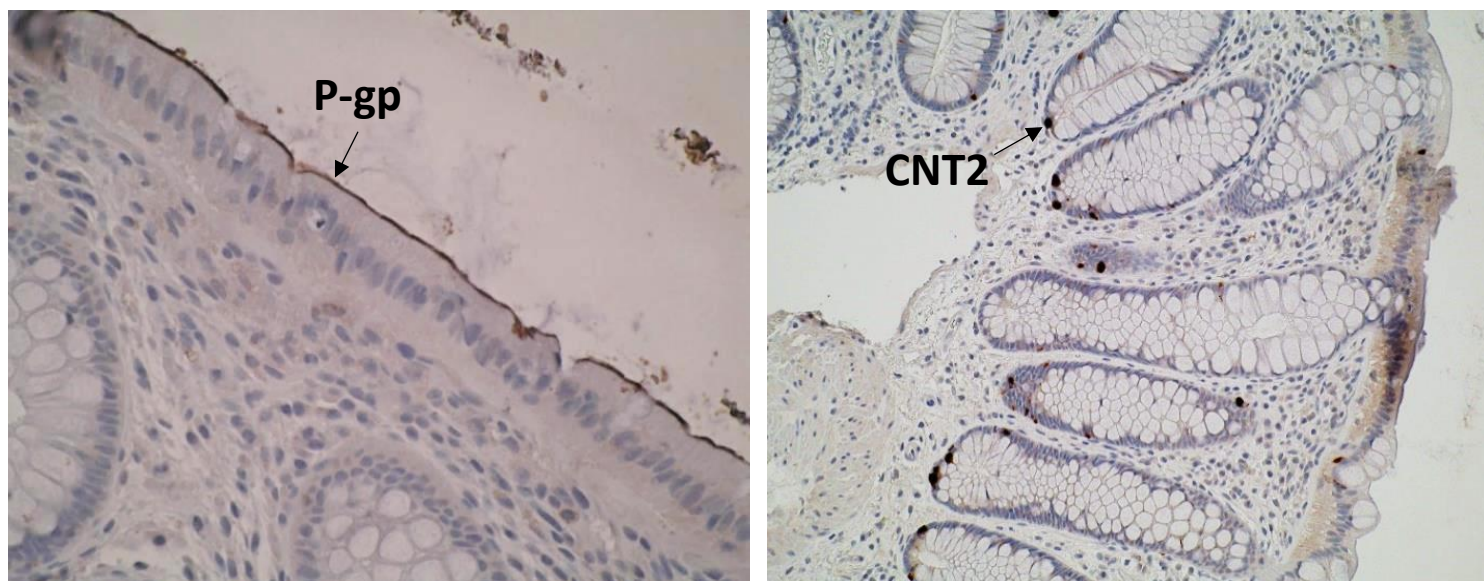


MOTIF: Description of main S&T results/foreground**Figures and Tables****Figure 1. Immunochemical detection of P-gp and CNT2 in colorectal tissue.****Table 1. Expression of 17 transporters key for distribution of ARV drugs investigated in human, macaque and rabbit cervicovaginal tissue.**

Drug Transporter	Macaque		Human			Rabbit
	Cervix	Vagina	Endocervix	Ectocervix	Vagina	Cervix/Vagina
P-gp	++ ^a	++	+ ^b	++	++	++
MRP1	++	++	+	++	++	++
MRP2	+	+	- ^c	+	-	+
MRP3	++	++	+	+	-	++
MRP4	++	++	+	+	-	++
MRP5	++	++	++	++	++	++
MRP6	+	-	-	+	-	-
BCRP	++	++	+	++	++	++
OCT1	-	-	-	+	-	+
OCT2	-	-	-	-	-	+
CNT1	-	-	-	+	-	+
CNT2	++	++	-	++	-	+
ENT1	++	++	++	++	++	++
ENT2	+	+	-	+	-	++
OATP2A1	++	++	++	++	++	++
OATP2B1	+	++	+	+	++	++
OATPD	+	++	+	+	++	+

^amean Ct of endogenous controls: mean Ct of transporter = 0.8-1 (moderate expression)^bmean Ct of endogenous controls: mean Ct of transporter <0.8 (low expression)^cnot expressed

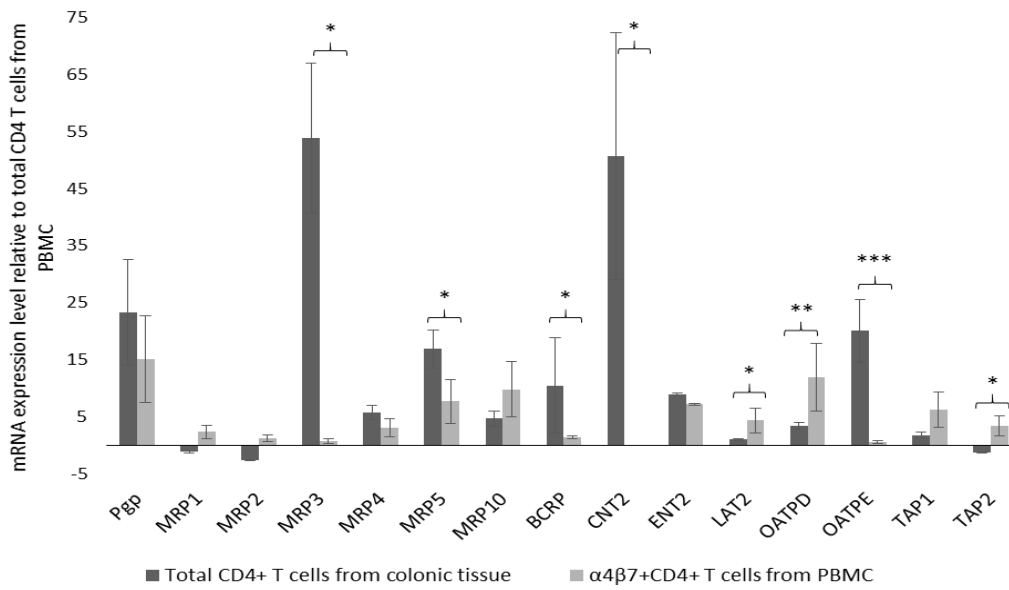


Figure 2. Comparison of drug transporter mRNA expression between colorectal CD4+ T cells, circulating $\alpha 4\beta 7+CD4+$ T cells and total CD4+ T cells isolated from PBMC.

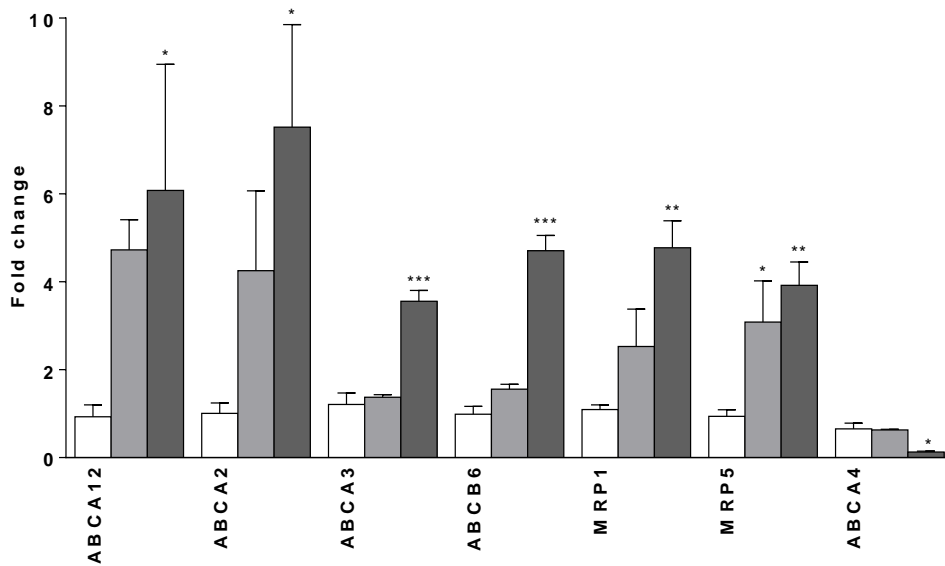


Fig 3. Efflux transporters gene expression in darunavir-treated HEC-1A cell lines.

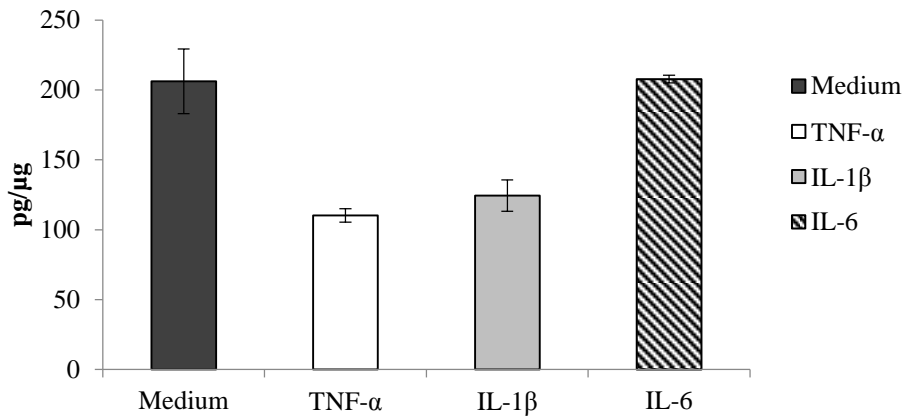


Figure 4. Intracellular accumulation of digoxin in VK2/E6E7 cells stimulated with TNF-α, IL-1β and IL-6.

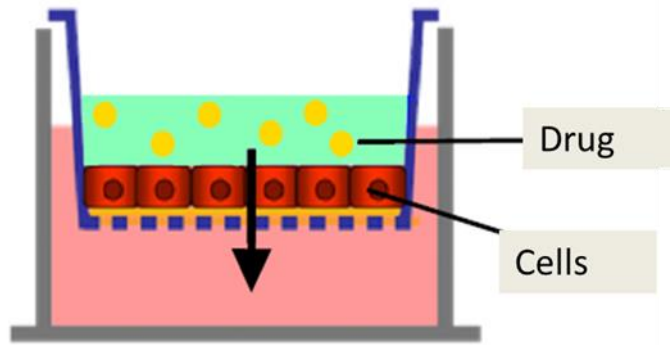


Figure 5. Diagram of the Transwell system showing drug transfer from apical to basolateral chambers.

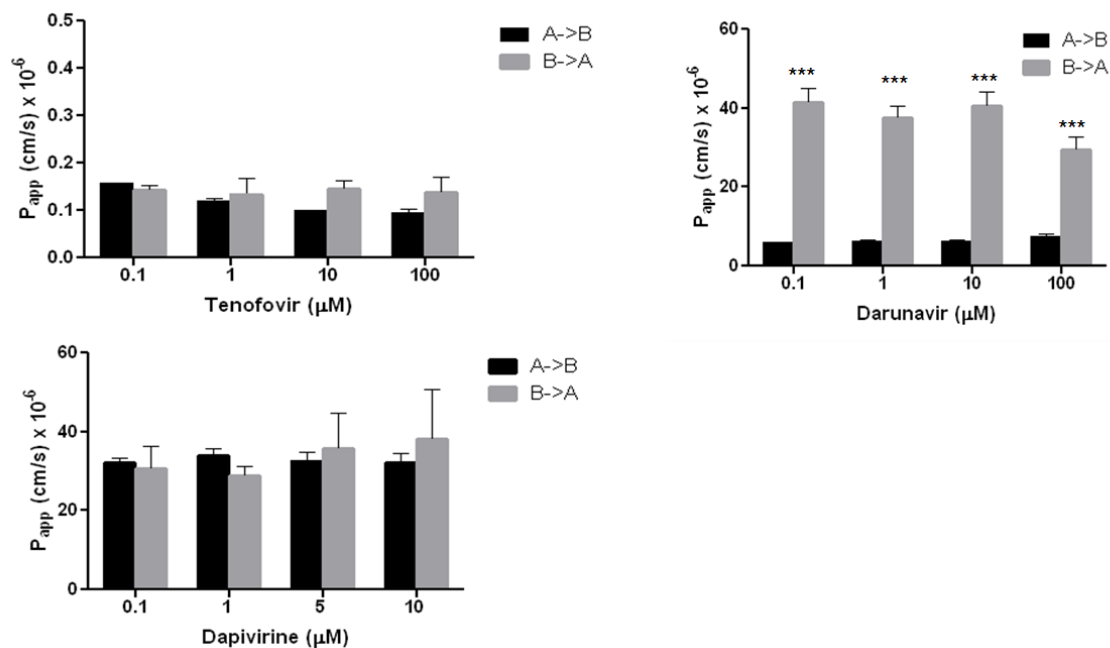


Figure 6. Caco-2: *in vitro* colorectal model. Concentration dependence of a) TFV (0.1-100μM), b)DAP (0.1-100μM), and c) DRV (0.1-10μM), permeability across Caco-2 cell monolayer in absorptive and secretory directions. Values represent the mean ± standard deviation from three independent studies performed in triplicate (*,p<0.001).**

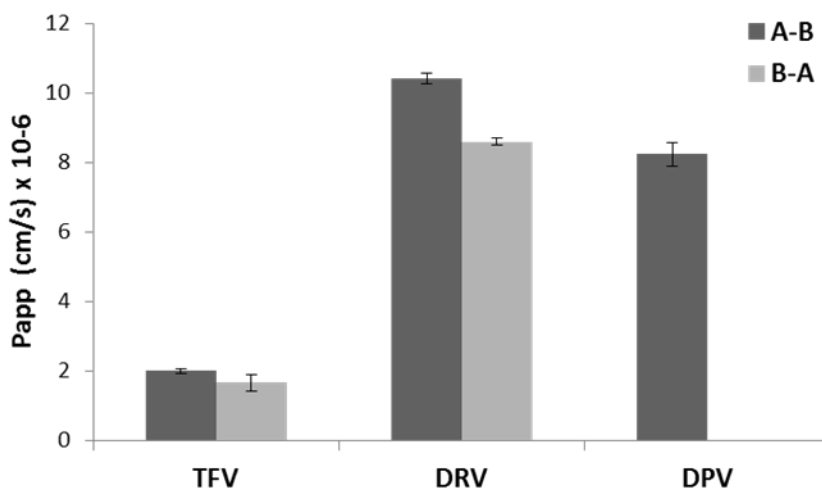


Figure 7. Permeability of tenofovir (TFV), darunavir (DRV) and dapivirine (DPV) across the HEC-1A model vaginal epithelium. Permeability of dapivirine (DPV) was only measured in the absorptive (A-B) direction since the presence of DMSO (required for dissolution of the drug) impaired integrity of the basolateral, but not the apical epithelial barrier.

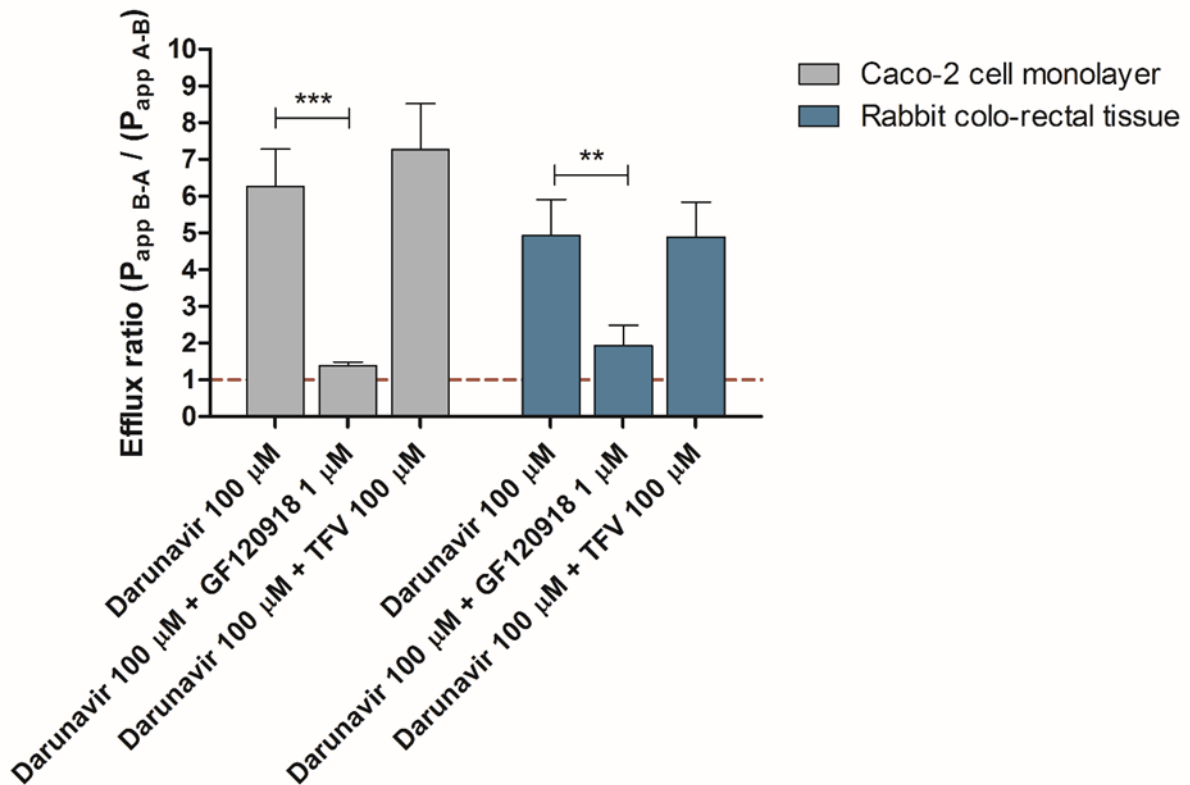





Figure 8. Permeability of Darunavir across Caco-2 barrier epithelium and Rabbit Colorectal Mucosa. In both models, effects of the Pgp inhibitor G120918 are similar and no drug-drug interaction with tenofovir is evident ($p < 0.001$; ** $p < 0.01$).**

Screen grabs of the MOTIF Project Website

The screenshot shows the MOTIF Project website homepage. At the top left is the MOTIF logo, which includes a red ribbon icon. To the right of the logo are five red navigation buttons: Project, Partners, Research, Newsroom, and Contact Us. Below the navigation is a 'Welcome to MOTIF project!' section with introductory text about the project's goals and timeline. A video player is embedded in this section, showing a woman speaking. Below the video is a quote from a partner, with a small profile picture of a man. At the bottom left is a 'Start Prezi' button with a magnifying glass icon. On the right side of the page, there is a search bar, a 'Leave your email here to stay in contact with us' form, a 'Twitter Updates' section with several tweets, and a 'Find us on Facebook' section with a Facebook post snippet. The footer contains a 'Partners Area' link and copyright information: 'Copyright © 2012 MOTIF. All rights reserved.'






Project Summary

What is MOTIF?




MOTIF is an acronym for Microbiode Optimization through Innovative Formulation for vaginal and rectal delivery. It is a collaborative project co-funded by the European Union under the 7th Framework Programme (FP7). MOTIF addresses the use of topical antiretroviral microbicides for the prevention of HIV infection.

The work to be undertaken in this project is complementary to that of an ongoing large scale collaborative project (CHAARIS - Combined Highly Active Anti-Retroviral Microbicides) which aims to develop novel microbicide combinations and to test their efficacy using in vitro and in vivo (IVRF) models.

The MOTIF investigation will last for 36 months and will end in September 2015.

To know more click [here!](#)

Who is MOTIF:



MOTIF is a small-medium scale collaborative project carried out by a consortium of 9 organizations coordinated by Professor Charles Kelly from King's College, London.

Have a look of [who else is involved.](#)

MOTIF aims to:

To develop innovative formulations that not only optimize drug delivery but also provide a generic procedure for combining ARVs even where drug physicochemical properties are potentially incompatible. It also aims to develop improved, physiologically relevant in vitro model systems to test microbicide formulations optimized for delivery to rectal or vaginal mucosae.

Read more about the [objectives and expected results.](#)







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Partners


MOTIF is a small-medium scale collaborative project carried out by a consortium of 9 organizations. The consortium includes 3 research active SMEs with specific expertise in formulation including production of clinical grade material, gene expression and in performing accredited ADMET studies as required by drug regulatory agencies. Minerva Consulting & Communication will act as dissemination partner. Other partners provide expertise in mucosal biology, gene expression and drug transport assays as well as extensive experience of pharmacokinetic and pharmacodynamic studies in the mouse model.

























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motif
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King's College London


KING'S College LONDON


King's College London is one of England's oldest and most prestigious universities. King's has played a major role in many of the advances that have shaped modern life, such as the discovery of the structure of DNA, and it is now the largest centre for the education of doctors, dentists and other healthcare professionals in Europe and home to an Medical Research Council Institute.

At MOTIF, we are pioneering innovation and the resources for developing in vivo systems to measure drug uptake and absorption. This includes use of established models of intestinal absorption but also developing new cellular models of mucosal epithelium. The Institute of Pharmaceutical Science is housed in Modern Sciences and includes a 30 M2 Cell Culture Unit with dedicated service support and a high cleanroom.

King's College is responsible for the overall management of the project and work packages WPI, WPI4, WPI7, WPI8.


Responsible Scientists


 Professor Charles Kelly is the coordinator of the MOTIF project and head of Oral Immunology in the Dental Institute. His research interests are in HIV pathogenesis and mucosal development. He is also coordinator of Dental project and was coordinator of EPRC.


 Dr. Ben Kebabian is a senior in Pharmaceutics and head of the Drug Delivery Group in the Institute of Pharmaceutical Science. He has pioneered the development of in vivo models of absorption, particularly enteric absorption, in novel oral drug delivery.


The Drug Delivery Group has excellent facilities for dosage form characterisation, secondary active formulation of dosage forms, and in vivo and in vitro evaluation of biopharmaceutical properties of drugs and medicines.


The following researchers supported absorption assays and bio-formulations, drug transport and drug-drug interactions as well as testing the effect of environmental changes on transport:

 Cheryl Angles – MOTIF project manager

 Akshay Kumar

 Hilda Zamboni

 Zeno Dovic

 Vitor Zilva

Partners

1. King's College London, UK
2. Novartis Biotech Inc., United States
3. MedTee s.r.l., Czech Republic
4. Micromedex s.r.l., Italy
5. Università degli Studi di Siena, Italy
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8. Commissariat à l'Énergie Atomique et aux Énergies Alternatives, France
9. Mithras Communication, Belgium

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