MOTIF: Description of main S&T results/foreground

Figures and Tables

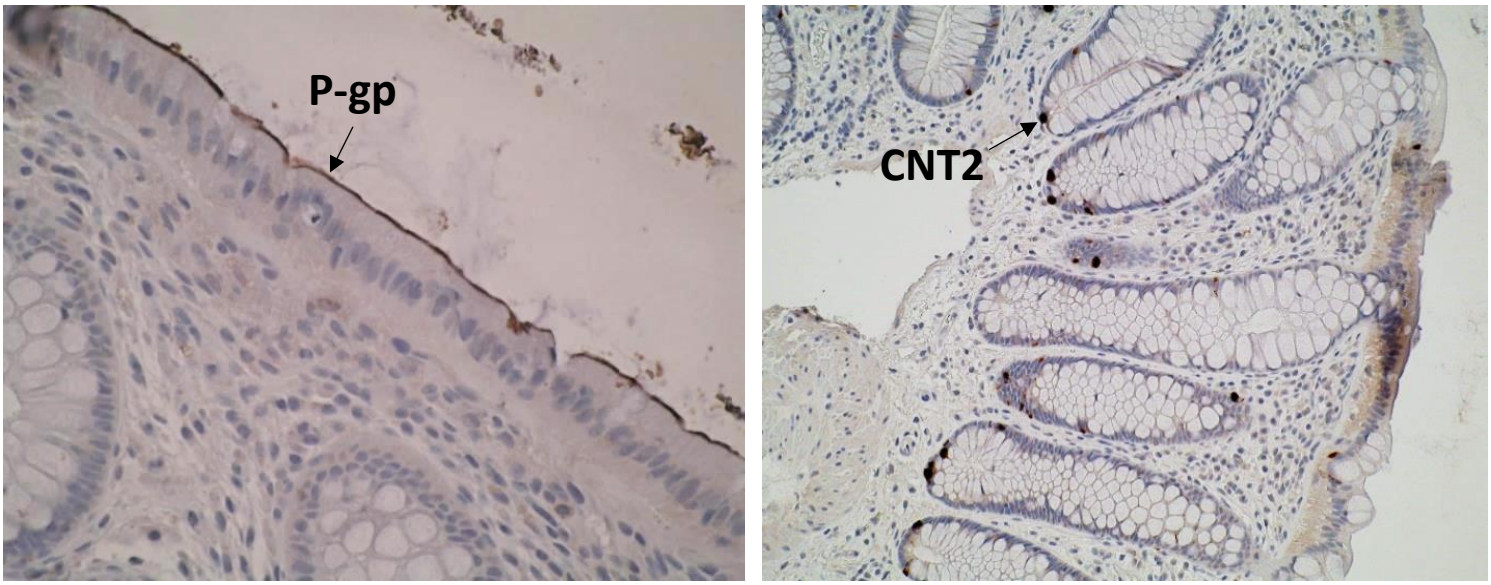

Figure 1. Immunochemical detection of P-gp and CNT2 in colorectal tissue.

Table 1. Expression of 17 transporters key for distribution of ARV drugs investigated in human, macaque and rabbit cervicovaginal tissue.

	Macaque		Human			Rabbit
Drug Transporter	**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	+	++	+	+	++	+

[a]mean Ct of endogenous controls: mean Ct of transporter = 0.8-1 (moderate expression)

[b]mean Ct of endogenous controls: mean Ct of transporter <0.8 (low expression)

[c]not expressed

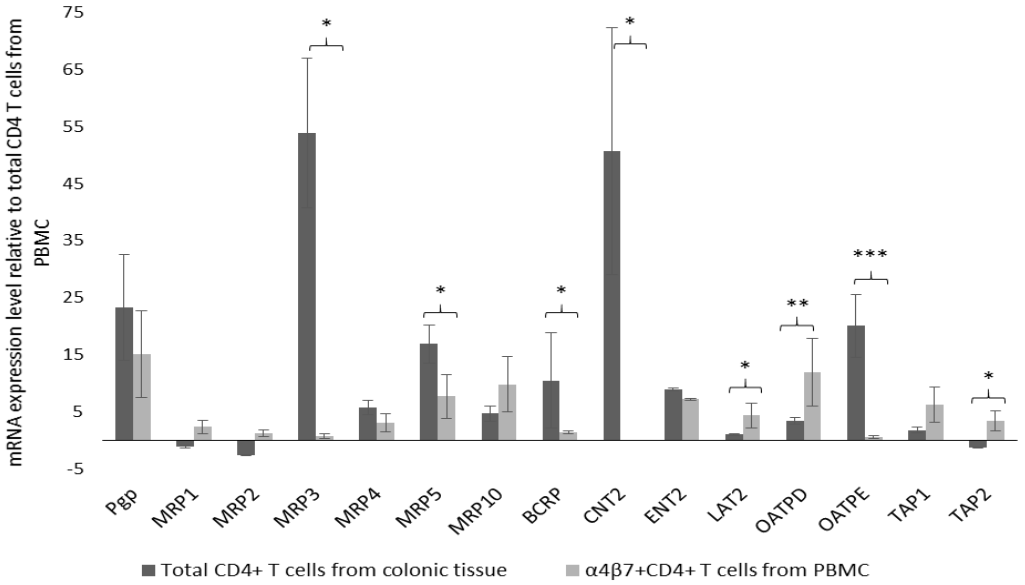

Figure 2. Comparison of drug transporter mRNA expression between colorectal CD4+ T cells, circulating α4β7+CD4+ T cells and total CD4+ T cells isolated from PBMC.

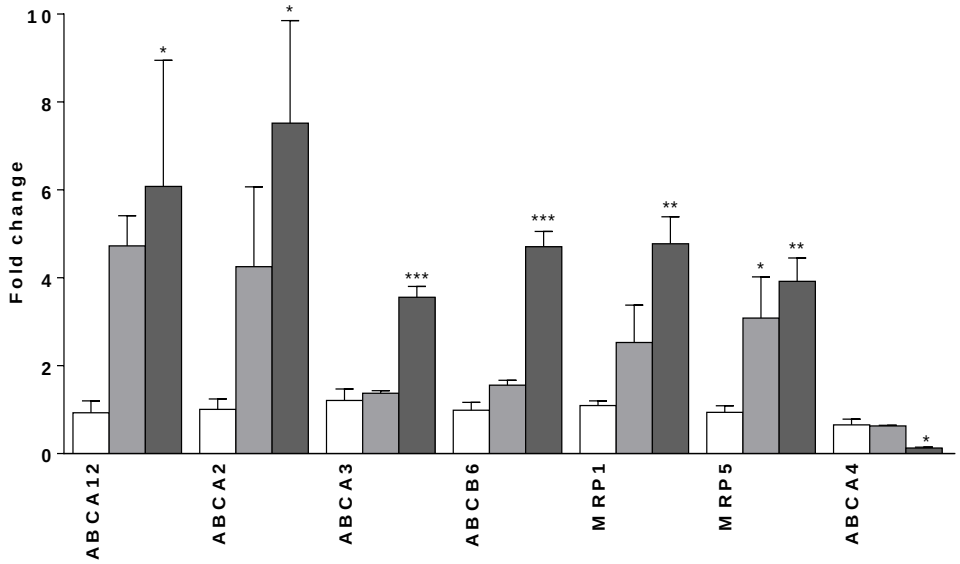

Fig 3. Efflux transporters gene expression in darunavir-treated HEC-1A cell lines.

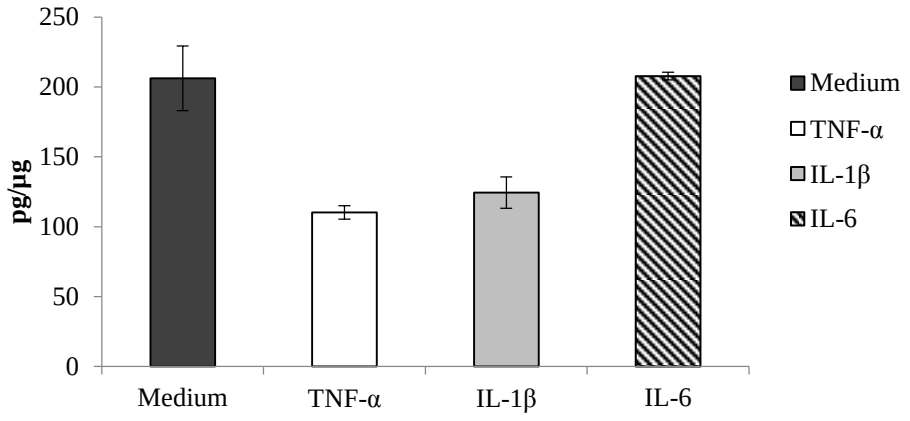

Figure 4. Intracellular accumulation of digoxin in VK2/E6E7 cells stimulated with TNF-α, IL-1β and IL-6.

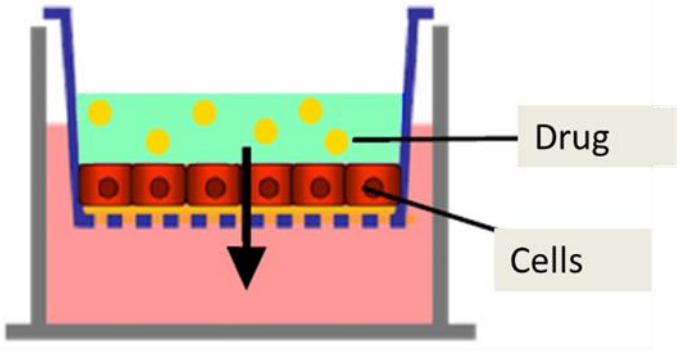

Figure 5. Diagram of the Transwell system showing drug transfer from apical to basolateral chambers.

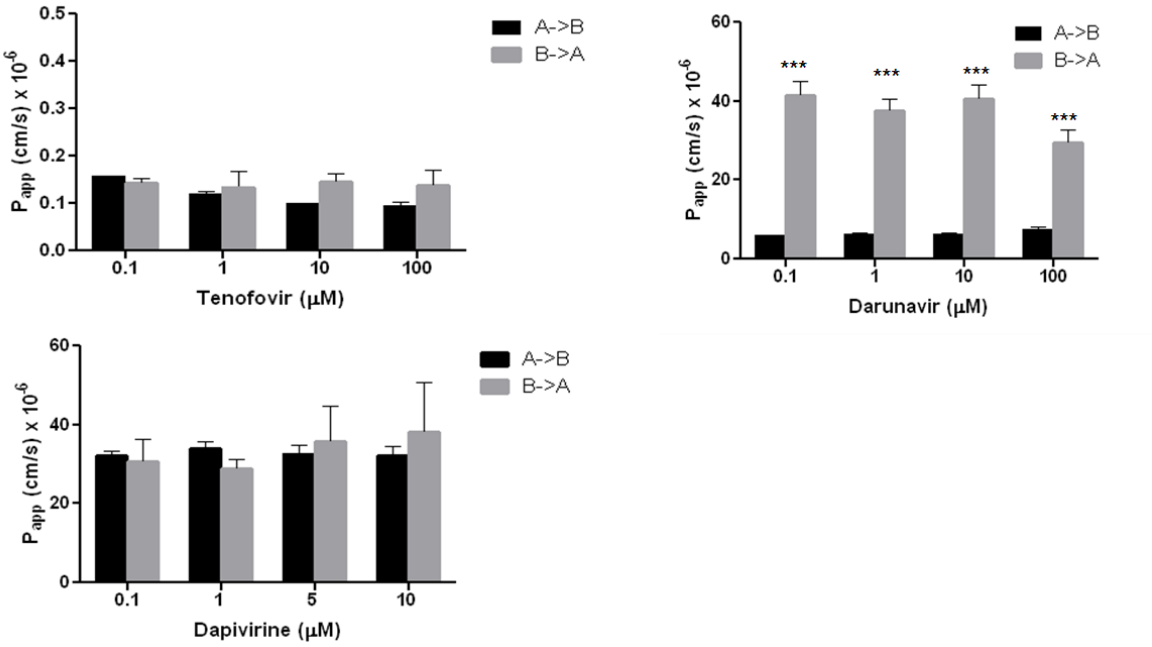

Figure 6. Caco-2: *in vitro* colorectal model. Concentration dependence of a) TFV (0.1-100µM), b)DAP (0.1-100µM), and c) DRV (0.1-10µM), permeability across Caco-2 cell monolayer in absorptive and secretory directions. Values represent the mean ± standard deviation from three independent studies performed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

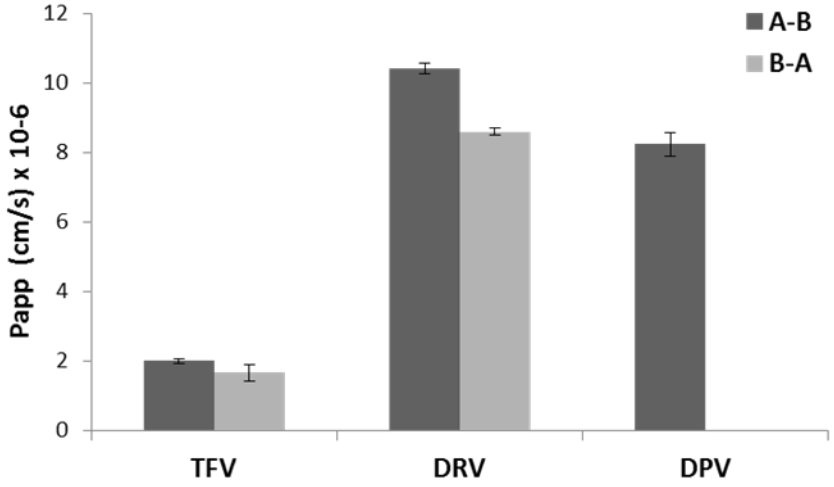

Figure 7. Permeability of tenofovir (TFV), darunavir (DRV) and dapivirine (DPV) across the HEC-1A model vaginal epithelium. Permeability of dapivirine (DPV) was only measured in the absorptive (A-B) direction since the presence of DMSO (required for dissolution of the drug) impaired integrity of the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

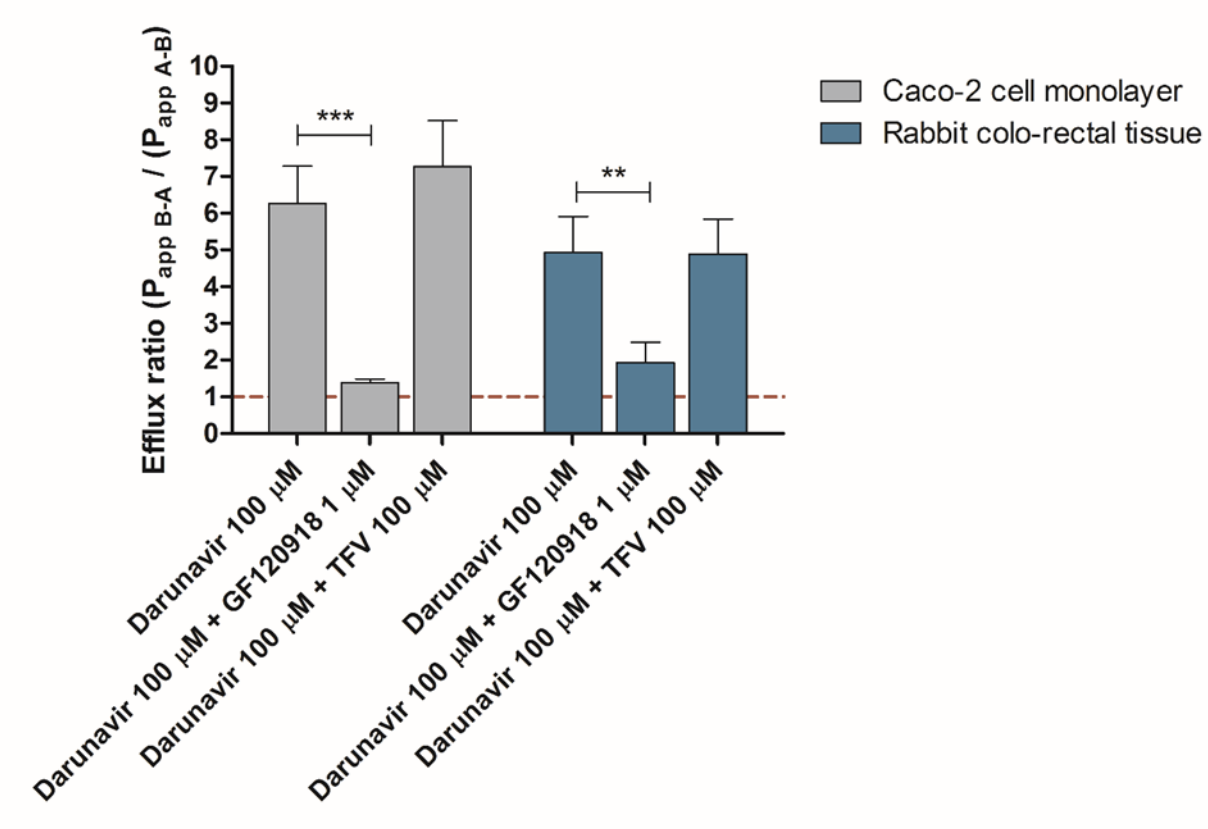

Figure 8. Permeability of Darunavir across Caco-2 barrier epithelium and Rabbit Colorectal Mucosa. In both models, effects of the Pgp inhibitor G120918 are similar and no drug-drug interaction with tenofovir is evident (* p<0.001; **p<0.01).**

Screen grabs of the MOTIF Project Website


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Project Summary
What is MOTIF?
MOTIF is an acronym for Microbicide 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 (CHAARM – Combined Highly Active Anti-Retroviral Microbicides) which aims to develop novel microbicide combinations and to test their efficacy using in vitro and in vivo (NHP) 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 optimise 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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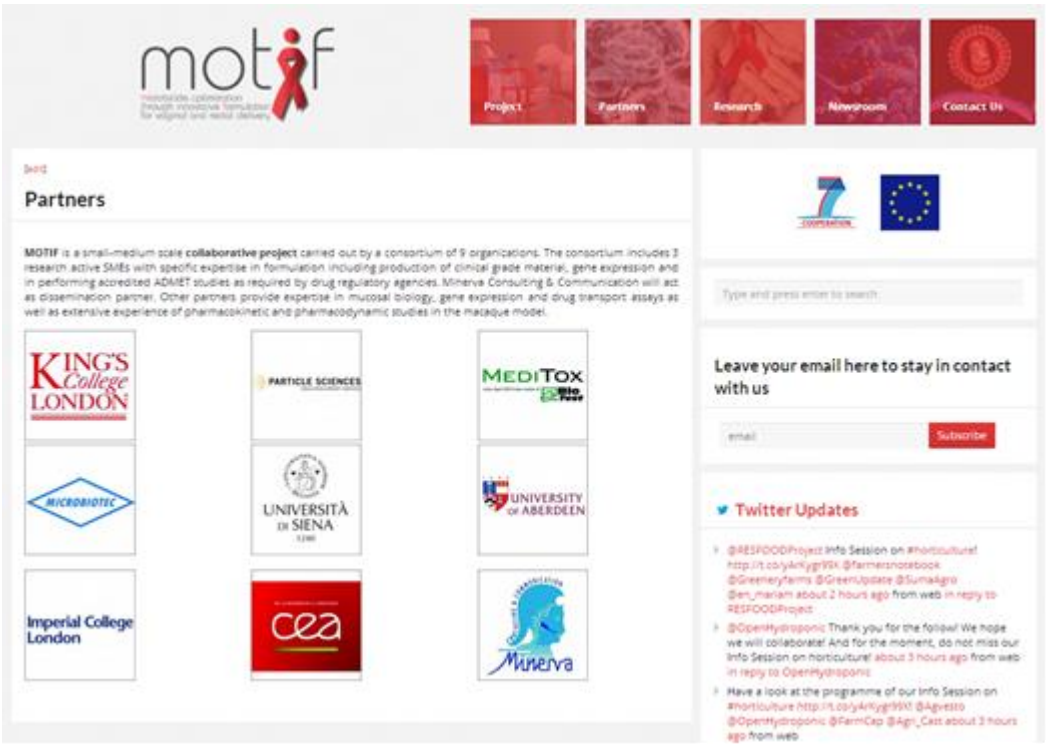
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MOTIF is a small-medium scale collaborative project carried out by a consortium of 9 organizations. The consortium includes 3 research active SMEs with specific expertise in formulation including production of clinical grade material, gene expression 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 macaque model.
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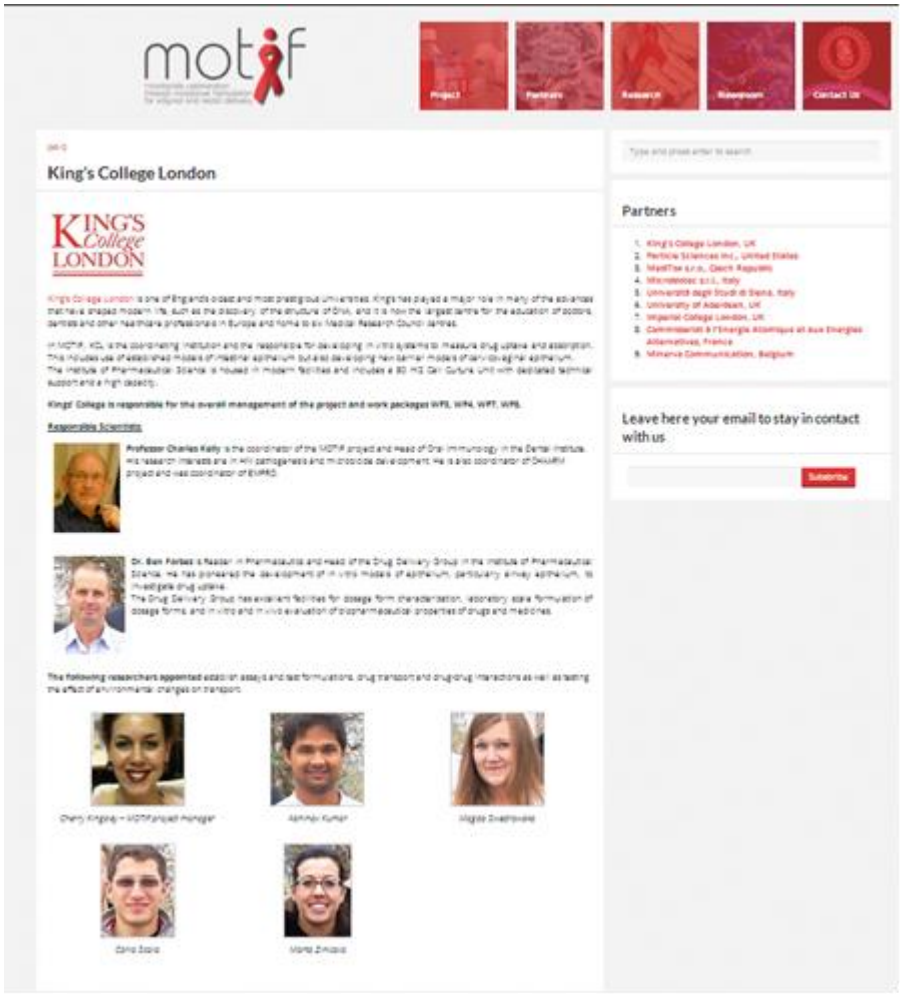
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