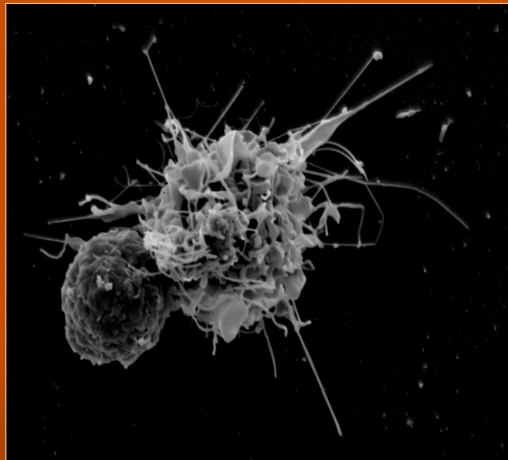
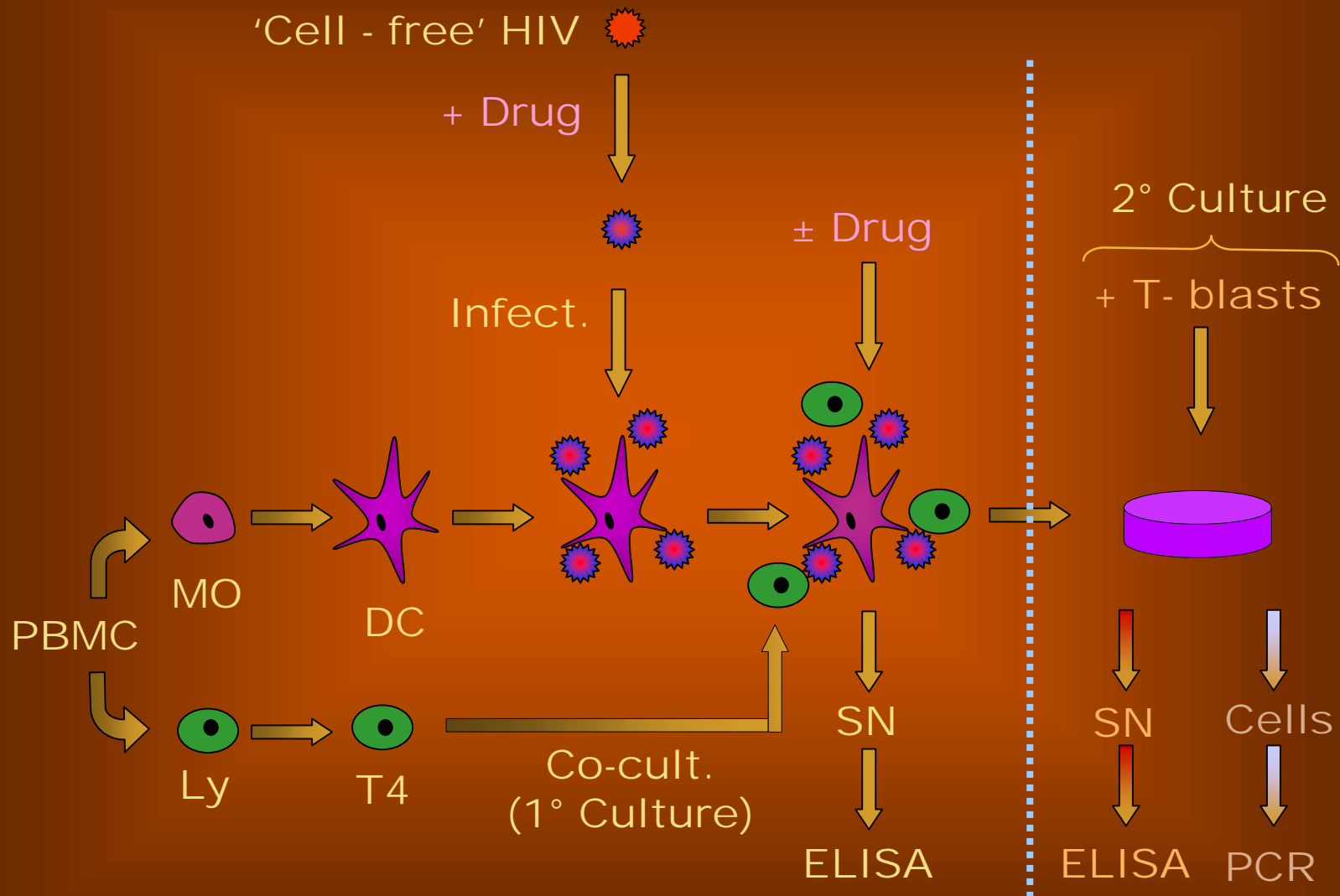




## Microbicidal activity of Dapivirine (TMC-120) and UC-781 in an in vitro Model for Prevention of Sexual HIV Transmission



## The MO-DC / T4 model with 'Cell-Free' HIV



## Anti-retroviral activity of Dapivirine and UC-781 on 'cell-free' HIV

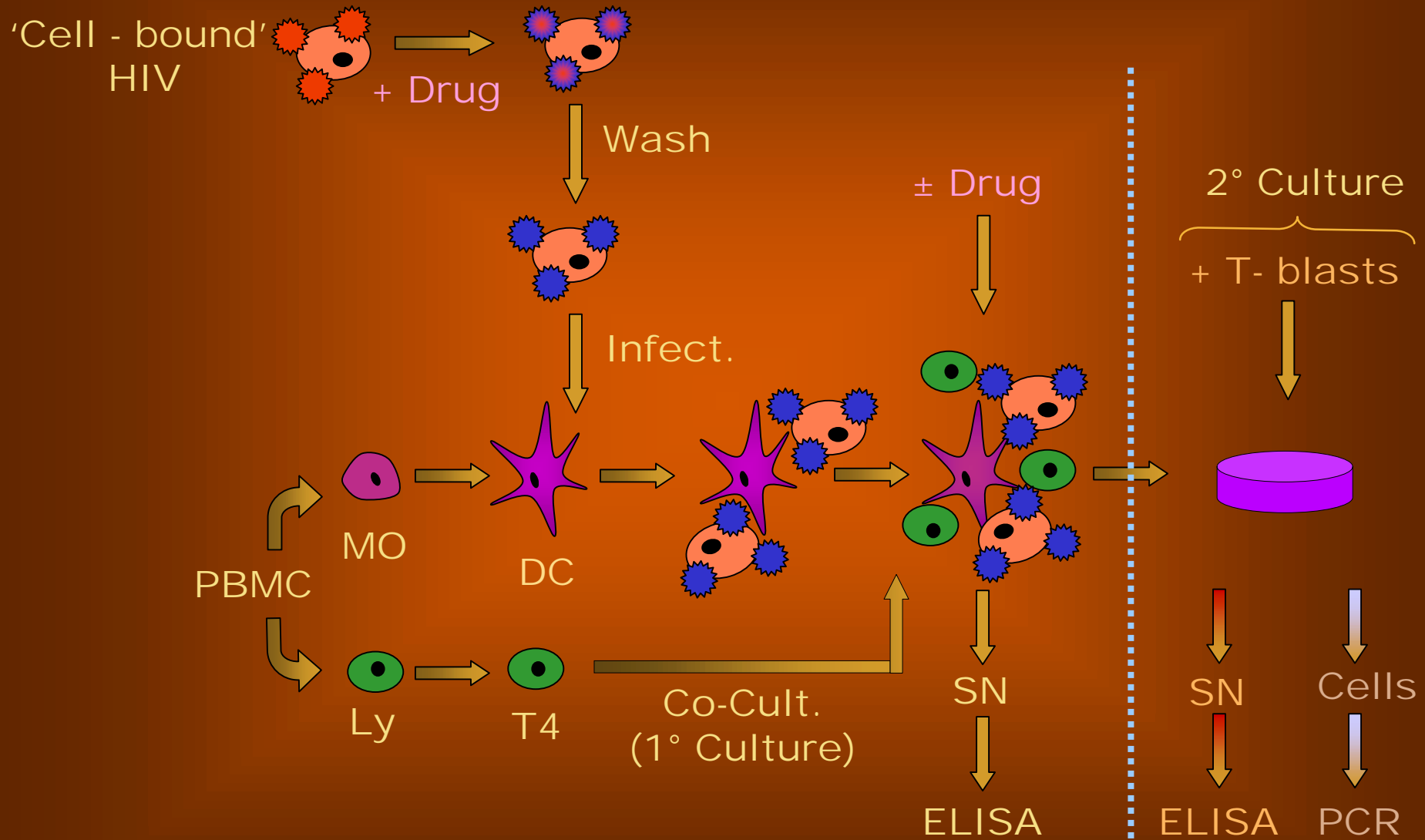
### 1) Drug present on HIV before and during infection (NOT after infection)

Drug	Conc. (nM)	HIV Ag (+) SN (1° Cult.)
UC-781	1000	5/6
	100	6
	10	6
	1	6
	0.1	6
Dapivirine	1000	4
	100	6
	10	6
	1	5
	0.1	6
No drug	0	6

2) “Maximal prevention”: Drug present before, during and after infection

Drug	Conc. (nM)	HIV Ag (+) SN		HIV DNA (2° Cult.)
		1° Cult.	2° Cult.	
UC-781	1000	0/6	1	5.01 Log
	100	0	2	4.76
	10	2	4	4.80
	1	6	6	ND
	0.1	6	6	ND
Dapivirine	1000	0	0	<b>Neg</b>
	100	0	0	<b>Neg</b>
	10	0	0	<b>Neg</b>
	1	0	2	4.76
	0.1	3	3	4.82
No drug	0	6	6	4.76

# The MO-DC / T4 model with 'Cell-Bound' HIV



## Anti-retroviral activity of Dapivirine and UC-781 on 'cell-bound' HIV

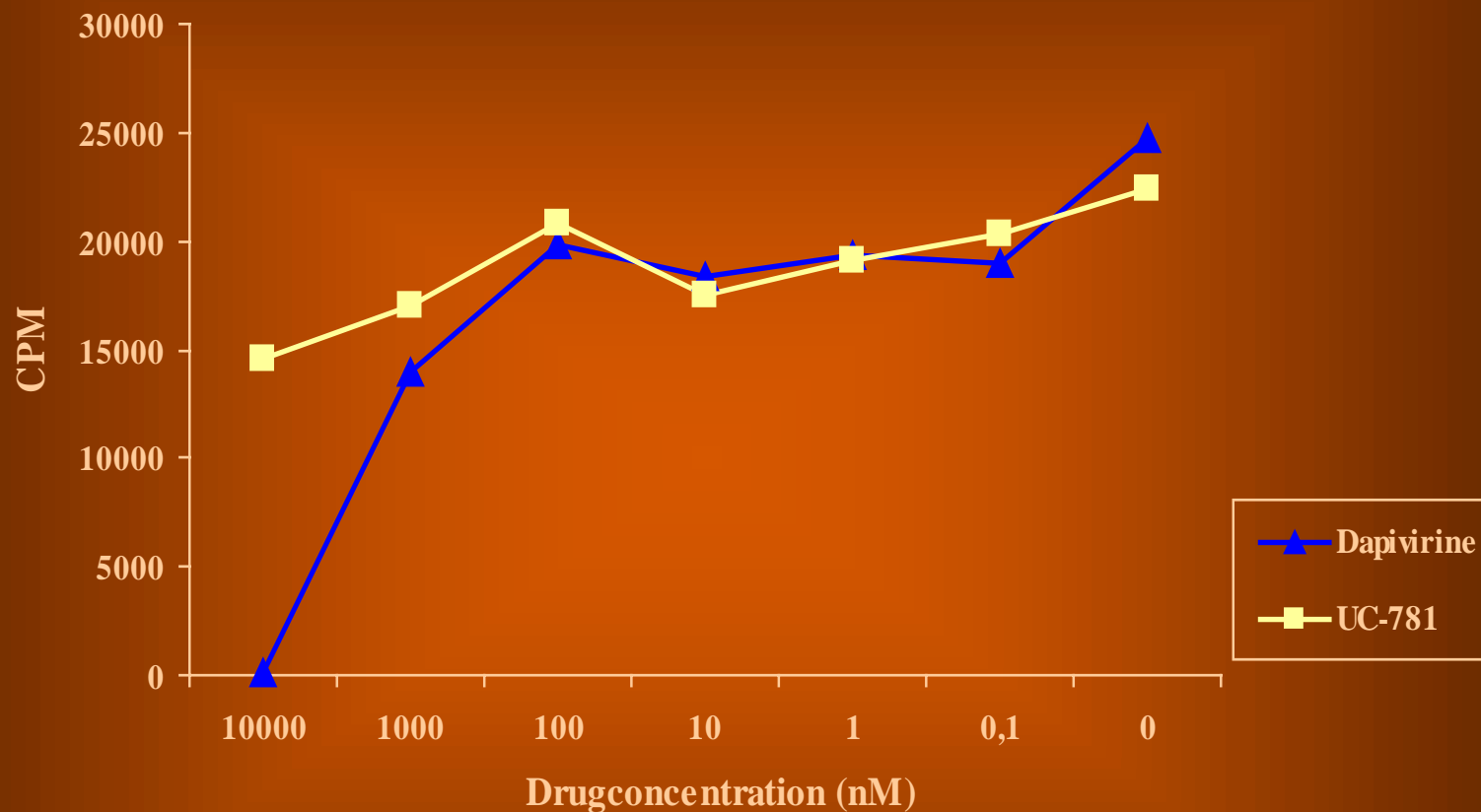
### 1) Drug present before infection (NOT during or after infection)

Drug	Conc. (nM)	HIV Ag (+) SN	
		1° Cult.	2° Cult.
UC-781	10.000	1/6	2
	1.000	6	6
	100	6	6
	10	6	6
Dapivirine	10.000	0/6	4
	1.000	4	5
	100	6	6
	10	6	6
No drug	0	6	6

## 2) Drug present before, during and after infection

Drug	Conc. (nM)	HIV Ag (+) SN		HIV DNA (2° Cult.)
		1° Cult.	2° Cult.	
UC-781	10.000	0/6	0	Neg
	1.000	0	1	4,66 Log
	100	0	4	ND
	10	5	5	ND
Dapivirine	10.000	0/6	0	Neg
	1.000	0	0	Neg
	100	0	0	Neg
	10	0	3	4,74 Log
No drug	0	6	6	4,85

## Immune-Suppressive Activity of Dapivirine and UC-781



**ISC<sub>50</sub> UC-781: > 10.000 nM**  
**Dapivirine: 886 nM**

## Summary:

We developed an *in vitro model* of monocyte-derived dendritic cells and autologous CD4(+) T cells for evaluating anti-retroviral drug potency.

Since both 'cell-free' and 'cell-bound' virus can be used and timing of drug treatment is adaptable, we propose this model as a suitable tool for microbicide research.

**Preliminary data concerning the use of UC-781 and Dapivirine were generated :**

- \* Short-term treatment (before and/or during infection) with UC-781 or Dapivirine is not very effective to abort infection with 'cell-free' or 'cell-bound' HIV.**
- \* Long-term treatment with UC-781 aborts viral replication at micromolar concentrations, in cells infected with 'cell-free' or 'cell-bound' HIV.**
- \* Long-term treatment with Dapivirine aborts viral replication in cells infected with 'cell-free' or 'cell-bound' HIV, at respectively 10 and 100 nM of Dapivirine.**
- \* Effective concentrations of both drugs are not immune-suppressive (no major inhibition of T-cell proliferation)**

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