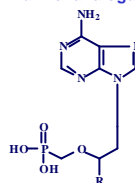


## Utilization des antiviraux pour les orthopoxvirus

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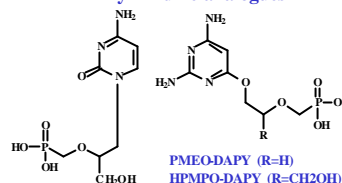
## ANPs

### Purine analogues



PMEA (R=H)  
(S)-HPMPA (R=CH<sub>2</sub>OH)

### Pyrimidine analogues



PMEO-DAPY (R=H)  
HPMPO-DAPY (R=CH<sub>2</sub>OH)

### Activity of selected ANPs against Vaccinia virus (Lederle strain) in HEL cells

Compound	IC <sub>50</sub> (µg/ml)	CC <sub>50</sub> (µg/ml)	MCC (µg/ml)	Selectivity index
HPMPC (Cidofovir)	3.57	37.9	>50	10.6
cHPMPC	4.74	>50	>50	>10.6
HPMPA	0.17	2.4	>20	14.1
3-deaza-HPMPA	0.78	3.2	20	4.1
cHPMPA	0.39	13.8	>20	35.4
HPMPDAP	0.51	25.3	>50	49.6
HPMPO-DAPY	0.76	10.9	>50	14.3
PMEA	>50	31.1	>50	<0.62
PMEDAP	>50	18.0	>50	<0.36
PMEO-DAPY	31.75	27.9	>50	0.88

### Activity of selected ANPs against Vaccinia virus (Lederle strain) in PHK cells

Compound	IC <sub>50</sub> (µg/ml)	CC <sub>50</sub> (µg/ml)	MCC (µg/ml)	Selectivity index
HPMPC (Cidofovir)	3.01	3.3	>50	1.1
cHPMPC	11.9	7.6	>50	0.64
HPMPA	0.92	1.3	>20	1.4
3-deaza-HPMPA	0.4	0.7	>20	1.8
cHPMPA	1.94	9.1	>20	4.7
HPMPDAP	0.84	3.4	>50	4.1
HPMPO-DAPY	1.55	6.3	>50	4.1
PMEA	>50	57.7	>50	<1.2
PMEDAP	26	6.4	>50	0.25
PMEO-DAPY	13.5	8.1	>50	0.6

### Activity of selected ANPs against Cowpox virus (Brighton strain) in HEL cells

Compound	IC <sub>50</sub> (µg/ml)	CC <sub>50</sub> (µg/ml)	MCC (µg/ml)	Selectivity index
HPMPC (Cidofovir)	4.6	37.9	>50	8.3
cHPMPC	4.33	>50	>50	>11.5
HPMPA	0.23	2.4	>20	10.7
3-deaza-HPMPA	2.31	3.2	20	1.37
cHPMPA	0.55	13.8	>20	25.4
HPMPDAP	0.75	25.3	>50	33.8
HPMPO-DAPY	1.65	10.9	>50	6.6
PMEA	>50	31.1	>50	<0.6
PMEDAP	>50	18.0	>50	<0.4
PMEO-DAPY	39.17	27.9	>50	<0.5

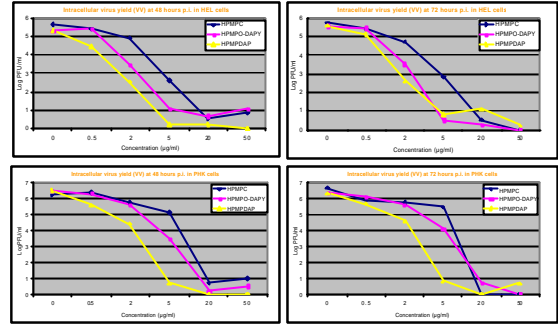
### Activity of selected ANPs against Cowpox virus (Brighton strain) in PHK cells

Compound	IC <sub>50</sub> (µg/ml)	CC <sub>50</sub> (µg/ml)	MCC (µg/ml)	Selectivity index
HPMPC (Cidofovir)	6.03	3.3	>50	0.6
cHPMPC	15.3	7.6	>50	0.5
HPMPA	1.69	1.3	>20	0.8
3-deaza-HPMPA	2.25	0.66	>20	0.3
cHPMPA	2.98	9.08	>20	3.0
HPMPDAP	1.56	3.43	>50	2.2
HPMPO-DAPY	2.86	6.27	>50	2.2
PMEA	>50	57.70	>50	<1.15
PMEDAP	>50	6.35	>50	<0.13
PMEO-DAPY	≈ 26.9	8.12	>50	≈ 0.3

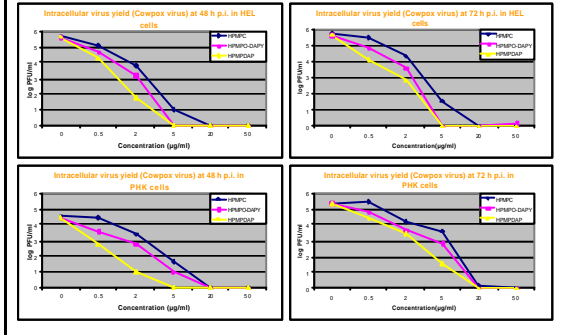
### Activity of selected ANPs against Orf virus (NZ2 strain)

Compound	IC <sub>50</sub> (µg/ml)	
	PLK cells	HEL cells
HPMPC	1.6	0.47
cHPMPC	5.3	1.3
HPMPA	0.69	0.13
3-cleaza-HPMPA	0.65	0.73
cHPMPA	1.12	0.26
HPMPDAP	1.9	0.47
HPMPO-DAPY	6.1	0.58
PMEA	> 50	> 50
PMEDAP	> 50	> 50
PMEO-DAPY	43.5	24.5

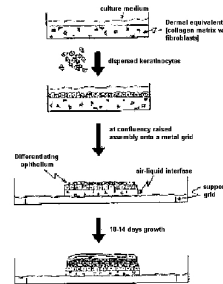
### Inhibition of intracellular virus yield (Vaccinia virus)



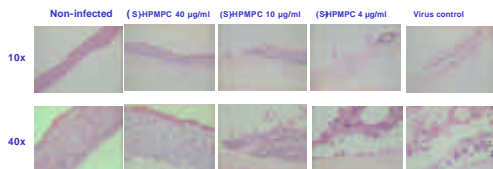
### Inhibition of intracellular virus yield (Cowpox virus)



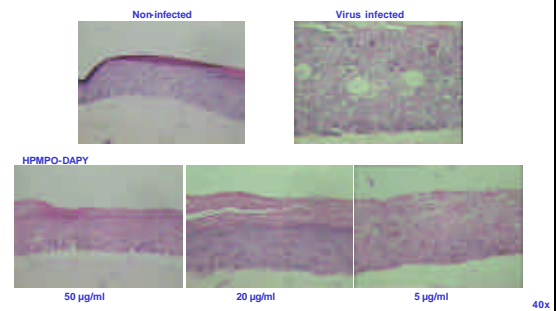
### Organotypic epithelial "raft" culture

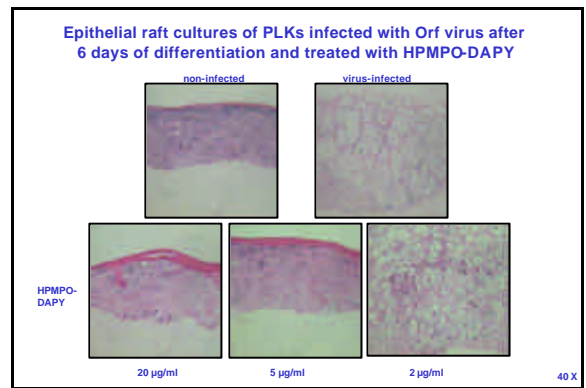
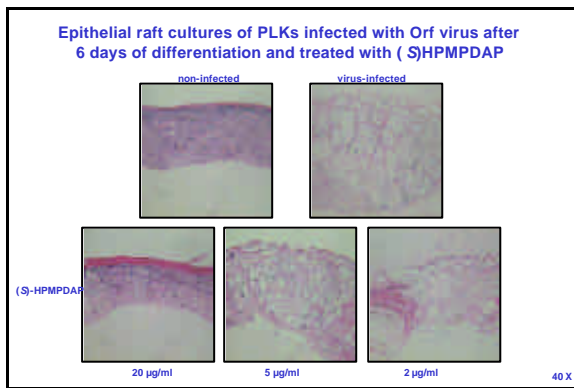
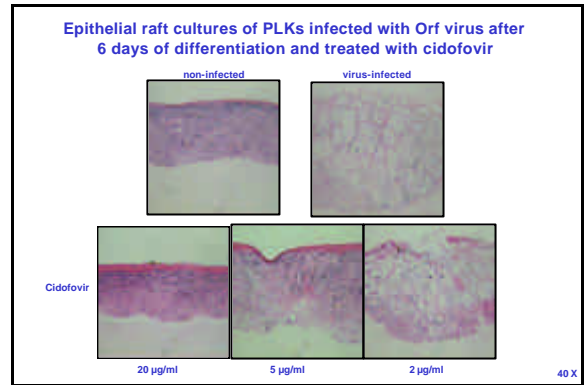
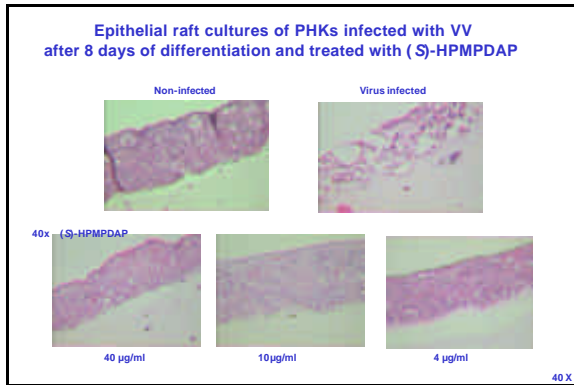


### Epithelial raft cultures of PHKs infected with VV after 6 days of differentiation and treated with cidofovir



### Epithelial raft cultures of PHKs infected with VV after 9 days of differentiation and treated with HPMPDAPY





**Activity of several ANPs against plaquepurified Vaccinia Virus mutants (strain Lederle) resistant to HPMPDAP in HEL cells**

Strain	Mean IC 50(µg/ml)							
	HPMPC	HPMPA	3-deaza-HPMPA	HPMPDAP	cHPMPC	cHPMPA	HPMPO-DAP	PMEO-DAP
HPMPC clone 1	15.5	0.69	0.74	2.3	23	1.67	9.6	24
HPMPC clone 2	11.5	0.7	0.57	2.3	14.5	1.33	6.7	21
HPMPC clone 3	16.5	1.8	1.27	9.13	30.8	7.72	15.3	26
HPMPC clone 4	14.9	1.75	1.01	6.23	25.5	6.85	7.7	21
HPMPC clone 5	15.9	1.3	1.17	7.2	28.8	5.72	8.3	28
HPMPC clone 6	15.1	0.91	0.88	5.9	27.4	6.13	9.0	31
HPMPC clone 7	13.0	1.17	1.0	5.6	23	4.36	4.2	21
wildtype clone 1	2.5	0.14	0.46	0.3	3.2	0.24	0.93	30
wildtype clone 2	1.8	0.095	0.32	0.28	3.9	0.39	0.9	25

**Activity of several ANPs against Vaccinia Virus mutants (strain Lederle) resistant to c-HPMPC, HPMPA and c-HPMPA in HEL cells**

Strain	Mean IC 50(µg/ml)						
	HPMPC	HPMPA	3-deaza-HPMPA	HPMPDAP	cHPMPC	cHPMPA	HPMPO-DAP
cHPMPC	6.7	1.13	0.55	5.7	14.2	3.6	14.7
HPMPA	6	0.96	0.46	4.5	14.8	2.2	7.4
c-HPMPA	7.6	1.45	0.32	4.2	7.5	2.3	7.0
3-deaza-HPMPA	2.4	0.14	0.61	0.4	5.3	0.38	0.9
wildtype	2.4	0.06	0.32	0.23	3.4	0.3	0.73

## Acknowledgements

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