

## **Electronic Supplementary Information**

### **Nano-SAR modeling for predicting the cytotoxicity of metal oxide nanoparticles to PaCa2**

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Table S1: List of chemicals conjugated to nanoparticles and their corresponding cellular uptake.  
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| ID                  | Name                                                            | PaCa2 cellular uptake<br>(log10 [nanoparticles]/cell<br>pM) | Prediction by<br>RF model |
|---------------------|-----------------------------------------------------------------|-------------------------------------------------------------|---------------------------|
| <b>Training set</b> |                                                                 |                                                             |                           |
| 1                   | trifluoroacetic anhydride                                       | 4.17                                                        | 1                         |
| 3                   | pentafluoropropanoic anhydride                                  | 4.08                                                        | 1                         |
| 5                   | furan-2,5-dione                                                 | 3.98                                                        | 1                         |
| 6                   | 3-methylfuran-2,5-dione                                         | 3.58                                                        | 0                         |
| 7                   | 3,4-dimethylfuran-2,5-dione                                     | 3.48                                                        | 1                         |
| 8                   | hexanoic anhydride                                              | 3.65                                                        | 0                         |
| 9                   | 3-methyl-dihydro-furan-2,5-dione                                | 3.64                                                        | 0                         |
| 10                  | 5,5'-carbonylbis(2-benzofuran-1,3-dione)                        | 3.51                                                        | 0                         |
| 11                  | 5-nitro-2-benzofuran-1,3-dione                                  | 3.27                                                        | 0                         |
| 13                  | 1,4,5,8-naphtalenetetracarboxylic anhydride                     | 3.67                                                        | 0                         |
| 14                  | 4,5,6,7-tetrafluoro-2-benzofuran-1,3-dione                      | 3.83                                                        | 1                         |
| 16                  | 4-hydroxy-2-benzofuran-1,3-dione                                | 3.97                                                        | 1                         |
| 17                  | 4-oxatricyclo[5.2.2.0 <sup>2,6</sup> ]undec-8-ene-3,5-dione     | 3.90                                                        | 1                         |
| 18                  | 6-chloro-2H-3,1-benzoxazine-2,4(1H)-dione                       | 4.18                                                        | 1                         |
| 19                  | 3H-2,1-benzoxathiol-3-one 1,1-dioxide                           | 3.88                                                        | 1                         |
| 20                  | 3,4-dichlorofuran-2,5-dione                                     | 3.84                                                        | 1                         |
| 21                  | S-(2,5-dioxotetrahydrofuran-3-yl) ethanethioate                 | 3.59                                                        | 0                         |
| 22                  | 5,6-dichloro-2-benzofuran-1,3-dione                             | 4.12                                                        | 1                         |
| 23                  | 4,10-dioxatricyclo[5.2.1.0 <sup>2,6</sup> ]dec-8-ene-3,5-dione  | 3.82                                                        | 1                         |
| 27                  | 6-nitro-1H,3H-benzo[de]isochromene-1,3-dione                    | 3.93                                                        | 1                         |
| 28                  | tetrahydrofuro[3',4':3,4]cyclobuta[1,2-c]furan-1,3,4,6-tetraone | 3.77                                                        | 1                         |
| 29                  | lauric anhydride                                                | 3.82                                                        | 1                         |
| 30                  | 1,3-dioxo-1,3-dihydro-2-benzofuran-5-carboxylic acid            | 3.55                                                        | 0                         |
| 31                  | 5-methyl-2-benzofuran-1,3-dione                                 | 3.98                                                        | 1                         |
| 32                  | 4-nitro-2-benzofuran-1,3-dione                                  | 3.50                                                        | 1                         |
| 33                  | 1H-isochromene-1,3(4H)-dione                                    | 3.78                                                        | 1                         |
| 34                  | dihydro-2H-pyran-2,6(3H)-dione                                  | 4.07                                                        | 1                         |
| 35                  | 4,4'-ethane-1,2-diyl dimorpholine-2,6-dione                     | 3.93                                                        | 1                         |
| 36                  | 2H-3,1-benzoxazine-2,4(1H)-dione                                | 4.44                                                        | 0                         |
| 37                  | 1-methyl-2H-3,1-benzoxazine-2,4(1H)-dione                       | 3.36                                                        | 1                         |
| 38                  | 4-methyldihydro-2H-pyran-2,6(3H)-dione                          | 3.91                                                        | 1                         |
| 39                  | 4,5,6,7-tetrahydro-2-benzofuran-1,3-dione                       | 3.73                                                        | 1                         |
| 40                  | 2,5-dioxotetrahydrofuran-3,4-diyl diacetate                     | 3.91                                                        | 1                         |
| 41                  | 4,5,6,7-tetrabromo-2-benzofuran-1,3-dione                       | 3.80                                                        | 0                         |
| 42                  | hexahydro-2-benzofuran-1,3-dione                                | 3.93                                                        | 0                         |
| 43                  | 5,6-dihydro-1H-cyclopenta[c]furan-1,3(4H)-dione                 | 3.69                                                        | 0                         |

|    |                                                                       |      |   |
|----|-----------------------------------------------------------------------|------|---|
| 44 | iodoacetic anhydride                                                  | 3.42 | 0 |
| 45 | chloroacetic anhydride                                                | 3.63 | 0 |
| 46 | 1,7,8,9,10,10-hexachloro-4-oxatricyclo[5.2.1.02,6]dec-8-ene-3,5-dione | 3.47 | 1 |
| 47 | Palmitic anhydride                                                    | 3.55 | 1 |
| 48 | 6-amino-1H,3H-benzo[de]isochromene-1,3-dione                          | 3.64 | 1 |
| 49 | Decanoic anhydride                                                    | 4.03 | 1 |
| 51 | 4-oxatricyclo[5.2.1.02,6]decane-3,5-dione                             | 3.94 | 1 |
| 52 | 1H,3H-benzo[de]isochromene-1,3-dione                                  | 3.96 | 1 |
| 54 | 4,5,6,7-tetrachloro-2-benzofuran-1,3-dione                            | 3.83 | 1 |
| 55 | 4,7-dichloro-2-benzofuran-1,3-dione                                   | 3.90 | 1 |
| 56 | 3,3-dimethyldihydro-2H-pyran-2,6(3H)-dione                            | 3.94 | 0 |
| 57 | pentan-1-amine                                                        | 3.78 | 1 |
| 58 | 4-methylpentan-2-amine                                                | 3.85 | 1 |
| 59 | 3-amino-6-(hydroxymethyl)cyclohexane-1,2,4-triol                      | 3.36 | 1 |
| 60 | hexan-1-amine                                                         | 3.75 | 1 |
| 61 | 2-methylpropan-2-amine                                                | 3.86 | 1 |
| 62 | 2-methylpropan-1-amine                                                | 3.72 | 0 |
| 63 | 2,2-dimethylpropan-1-amine                                            | 3.75 | 1 |
| 66 | 2-methylbutan-2-amine                                                 | 4.07 | 0 |
| 67 | ethane-1,2-diamine                                                    | 3.46 | 0 |
| 68 | pentadecan-1-amine                                                    | 4.06 | 1 |
| 70 | butane-1,4-diamine                                                    | 3.48 | 1 |
| 71 | hexane-1,6-diamine                                                    | 3.62 | 0 |
| 72 | 2-ethylhexan-1-amine                                                  | 3.95 | 1 |
| 73 | 1-hexadecylamine                                                      | 3.97 | 0 |
| 74 | heptan-2-amine                                                        | 3.63 | 0 |
| 75 | tetradecan-1-amine                                                    | 4.27 | 0 |
| 76 | N-(2-aminoethyl)ethane-1,2-diamine                                    | 3.77 | 0 |
| 77 | 1-(tricyclo[3.3.1.13,7]dec-1-yl)methanamine                           | 2.84 | 0 |
| 78 | 4-(2-aminoethyl)benzene-1,2-diol                                      | 2.53 | 0 |
| 79 | 4-(2-aminoethyl)phenol                                                | 2.77 | 0 |
| 80 | N-(2-aminoethyl)-N'-(3-aminopropyl)butane-1,4-diamine                 | 2.41 | 0 |
| 81 | N,N'-bis(2-aminoethyl)propane-1,3-diamine                             | 2.23 | 0 |
| 82 | 3,6,9,12-tetraazatetradecane-1,14-diamine                             | 2.54 | 0 |
| 83 | tricyclo[3.3.1.03,7]nonan-3-amine                                     | 3.12 | 0 |
| 84 | tricyclo[3.3.1.13,7]decan-2-amine                                     | 3.18 | 0 |
| 85 | aminoacetic acid                                                      | 2.57 | 0 |
| 86 | methyl 2-amino-3-phenylpropanate                                      | 3.39 | 0 |
| 88 | 2-amino-3-hydroxybutanoic acid                                        | 3.21 | 0 |
| 89 | 2-amino-3-(1H-indol-3-yl)propanoic acid                               | 3.19 | 0 |
| 95 | 2-amino-5-carbamimidamidopentanoic acid                               | 3.15 | 0 |
| 96 | 2-aminobutanedioic acid                                               | 3.29 | 0 |
| 97 | 2,5-diamino-5-oxopentanoic acid                                       | 3.32 | 0 |

|                 |                                                         |      |   |
|-----------------|---------------------------------------------------------|------|---|
| 98              | 2-aminopentanedioic acid                                | 3.40 | 0 |
| 99              | 2-amino-3-(1H-imidazol-4-yl)propanoic acid              | 3.38 | 0 |
| 100             | 2-amino-4-(methylsulfanyl)butanoic acid                 | 3.23 | 0 |
| 101             | 2-amino-3-phenylpropanoic acid                          | 3.29 | 0 |
| 102             | dihydrofuran-2,5-dione                                  | 4.24 | 1 |
| 103             | acetic anhydride                                        | 4.05 | 1 |
| 104             | 3-methylidenedihydrofuran-2,5-dione                     | 4.04 | 1 |
| 105             | 1,4-dioxane-2,6-dione                                   | 3.99 | 1 |
| 106             | 2-benzofuran-1,3-dione                                  | 3.90 | 1 |
| 107             | (2,5-dioxotetrahydrofuran-3-yl)acetic acid              | 4.03 | 1 |
| <b>Test set</b> |                                                         |      |   |
| 2               | chloro(difluoro)acetic anhydride                        | 3.95 | 1 |
| 4               | 3,3-dimethyldihydrofuran-2,5-dione                      | 4.11 | 1 |
| 12              | 6-bromo-1H,3H-benzo[de]isochromene-1,3-dione            | 3.63 | 0 |
| 15              | 5-nitro-1H,3H-benzo[de]isochromene-1,3-dione            | 4.11 | 1 |
| 24              | oct-7-ene-2,3,5,6-tetracarboxylic anhydride             | 3.63 | 0 |
| 25              | 3a,4,7,7a-tetrahydro-2-benzofuran-1,3-dione             | 3.89 | 1 |
| 26              | dibenzo[c,e]oxepine-5,7-dione                           | 3.77 | 1 |
| 50              | 8-oxaspiro[4.5]decane-7,9-dione                         | 4.06 | 0 |
| 53              | 3-phenyldihydro-2H-pyran-2,6(3H)-dione                  | 4.02 | 0 |
| 64              | 3-methylbutan-1-amine                                   | 3.83 | 0 |
| 65              | pentan-3-amine                                          | 3.81 | 1 |
| 69              | propane-1,3-diamine                                     | 3.49 | 1 |
| 87              | 2-amino-3-hydroxypropanoic acid                         | 3.36 | 1 |
| 90              | 2-amino-3-(4-hydroxyphenyl)propanoic acid               | 3.07 | 1 |
| 91              | 2-amino-3-methylbutanoic acid                           | 3.27 | 0 |
| 92              | 2,6-diaminohexanoic acid                                | 3.25 | 0 |
| 93              | amino(4-chlorophenyl)acetic acid                        | 3.06 | 0 |
| 94              | 2-aminopropanoic acid                                   | 2.90 | 0 |
| 108             | 4,7-difluoro-2-benzofuran-1,3-dione                     | 3.91 | 1 |
| 109             | {bis[2-(2,6-dioxomorpholin-4-yl)ethyl]amino}acetic acid | 4.10 | 0 |