

## **Discovery of novel 1,2,3-triazole derivatives as anticancer agents using QSAR and *in silico* structural modification**

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**Table S2** Predicted cytotoxic activity (pIC<sub>50</sub>) of modified compounds (**1A-1R**, **2A-2R**, **7A-7R** and **8A-8R**) and experimental cytotoxic activity of reference drugs

| Compound  | pIC <sub>50</sub>   |                       |                     |                     |
|-----------|---------------------|-----------------------|---------------------|---------------------|
|           | HuCCA-1             | HepG2                 | A549                | MOLT-3              |
| <b>1A</b> | -1.731 <sup>c</sup> | -1.652 <sup>c</sup>   | -1.027 <sup>c</sup> | -0.915 <sup>b</sup> |
| <b>1B</b> | -2.319 <sup>c</sup> | -1.067 <sup>c</sup>   | -1.083 <sup>c</sup> | -1.087 <sup>c</sup> |
| <b>1C</b> | -1.563 <sup>c</sup> | -1.254 <sup>c</sup>   | -1.091 <sup>c</sup> | -0.687 <sup>b</sup> |
| <b>1D</b> | -1.983 <sup>c</sup> | -1.285 <sup>c</sup>   | -0.931 <sup>b</sup> | -1.543 <sup>c</sup> |
| <b>1E</b> | -1.395 <sup>c</sup> | -1.222 <sup>c</sup>   | -0.954 <sup>b</sup> | -1.542 <sup>c</sup> |
| <b>1F</b> | -2.067 <sup>c</sup> | -0.791 <sup>b</sup>   | -1.125 <sup>c</sup> | -0.933 <sup>b</sup> |
| <b>1G</b> | -2.235 <sup>c</sup> | -0.846 <sup>b</sup>   | -1.061 <sup>c</sup> | -0.697 <sup>b</sup> |
| <b>1H</b> | -1.395 <sup>c</sup> | -1.073 <sup>c</sup>   | -0.931 <sup>b</sup> | -1.388 <sup>c</sup> |
| <b>1J</b> | -1.311 <sup>c</sup> | -1.104 <sup>c</sup>   | -1.184 <sup>c</sup> | -0.864 <sup>b</sup> |
| <b>1K</b> | -1.731 <sup>c</sup> | -0.421 <sup>b</sup>   | -1.187 <sup>c</sup> | -0.910 <sup>b</sup> |
| <b>1L</b> | -1.563 <sup>c</sup> | -0.809 <sup>b</sup>   | -1.184 <sup>c</sup> | -0.604 <sup>b</sup> |
| <b>1M</b> | -3.075 <sup>c</sup> | -0.895 <sup>b</sup>   | -1.149 <sup>c</sup> | -1.387 <sup>c</sup> |
| <b>1N</b> | -1.647 <sup>c</sup> | -0.369 <sup>b</sup>   | -1.168 <sup>c</sup> | -0.980 <sup>b</sup> |
| <b>1P</b> | -1.563 <sup>c</sup> | -0.151 <sup>b,d</sup> | -1.259 <sup>c</sup> | -0.507 <sup>b</sup> |
| <b>1Q</b> | -1.898 <sup>c</sup> | -0.290 <sup>b</sup>   | -1.195 <sup>c</sup> | -0.386 <sup>b</sup> |
| <b>1R</b> | -2.319 <sup>c</sup> | -0.590 <sup>b</sup>   | -1.196 <sup>c</sup> | -1.575 <sup>c</sup> |
| <b>2A</b> | -1.815 <sup>c</sup> | -1.773 <sup>c</sup>   | -1.815 <sup>c</sup> | -1.253 <sup>c</sup> |
| <b>2B</b> | -1.647 <sup>c</sup> | -0.990 <sup>b</sup>   | -1.697 <sup>c</sup> | -1.008 <sup>c</sup> |
| <b>2C</b> | -1.479 <sup>c</sup> | -1.184 <sup>c</sup>   | -1.697 <sup>c</sup> | -1.031 <sup>c</sup> |
| <b>2D</b> | -1.479 <sup>c</sup> | -1.554 <sup>c</sup>   | -1.844 <sup>c</sup> | -1.654 <sup>c</sup> |
| <b>2E</b> | -1.395 <sup>c</sup> | -1.234 <sup>c</sup>   | -1.791 <sup>c</sup> | -1.629 <sup>c</sup> |
| <b>2F</b> | -1.563 <sup>c</sup> | -0.937 <sup>b</sup>   | -1.729 <sup>c</sup> | -0.720 <sup>b</sup> |
| <b>2G</b> | -2.067 <sup>c</sup> | -0.635 <sup>b</sup>   | -1.687 <sup>c</sup> | -1.063 <sup>c</sup> |
| <b>2H</b> | -1.311 <sup>c</sup> | -1.243 <sup>c</sup>   | -1.796 <sup>c</sup> | -1.879 <sup>c</sup> |
| <b>2J</b> | -1.647 <sup>c</sup> | -1.679 <sup>c</sup>   | -2.075 <sup>c</sup> | -1.211 <sup>c</sup> |
| <b>2K</b> | -1.479 <sup>c</sup> | -0.979 <sup>b</sup>   | -1.895 <sup>c</sup> | -1.175 <sup>c</sup> |
| <b>2L</b> | -1.563 <sup>c</sup> | -1.069 <sup>c</sup>   | -1.892 <sup>c</sup> | -1.063 <sup>c</sup> |
| <b>2M</b> | -3.327 <sup>c</sup> | -1.663 <sup>c</sup>   | -2.128 <sup>c</sup> | -1.560 <sup>c</sup> |

<sup>a</sup> Highly active compound. <sup>b</sup> Moderately active compound. <sup>c</sup> Weakly active to inactive compound. <sup>d</sup> The most potent compound against each cancer cell line. <sup>e</sup> Not tested. <sup>f</sup> Experimental pIC<sub>50</sub> values.

**Table S2** Predicted cytotoxic activity (pIC<sub>50</sub>) of modified compounds (**1A-1R**, **2A-2R**, **7A-7R** and **8A-8R**) and experimental cytotoxic activity of reference drugs (continue)

| Compound  | pIC <sub>50</sub>   |                     |                       |                     |
|-----------|---------------------|---------------------|-----------------------|---------------------|
|           | HuCCA-1             | HepG2               | A549                  | MOLT-3              |
| <b>2N</b> | -1.563 <sup>c</sup> | -0.622 <sup>b</sup> | -2.061 <sup>c</sup>   | -1.317 <sup>c</sup> |
| <b>2P</b> | -1.563 <sup>c</sup> | -0.844 <sup>b</sup> | -1.924 <sup>c</sup>   | -0.356 <sup>b</sup> |
| <b>2Q</b> | -1.395 <sup>c</sup> | -0.687 <sup>b</sup> | -1.887 <sup>c</sup>   | -0.980 <sup>b</sup> |
| <b>2R</b> | -1.227 <sup>c</sup> | -1.451 <sup>c</sup> | -2.066 <sup>c</sup>   | -2.171 <sup>c</sup> |
| <b>7A</b> | -3.159 <sup>c</sup> | -1.400 <sup>c</sup> | -1.538 <sup>c</sup>   | -0.424 <sup>b</sup> |
| <b>7B</b> | -3.243 <sup>c</sup> | -0.790 <sup>b</sup> | -1.505 <sup>c</sup>   | -0.535 <sup>b</sup> |
| <b>7C</b> | -3.495 <sup>c</sup> | -1.037 <sup>c</sup> | -1.516 <sup>c</sup>   | -0.187 <sup>b</sup> |
| <b>7D</b> | -3.915 <sup>c</sup> | -1.348 <sup>c</sup> | -1.545 <sup>c</sup>   | -1.226 <sup>c</sup> |
| <b>7E</b> | -2.991 <sup>c</sup> | -1.073 <sup>c</sup> | -1.500 <sup>c</sup>   | -0.573 <sup>b</sup> |
| <b>7F</b> | -2.907 <sup>c</sup> | -0.163 <sup>b</sup> | -1.534 <sup>c</sup>   | -0.133 <sup>b</sup> |
| <b>7G</b> | -2.991 <sup>c</sup> | -0.562 <sup>b</sup> | -1.500 <sup>c</sup>   | 0.155 <sup>a</sup>  |
| <b>7H</b> | -3.075 <sup>c</sup> | -1.034 <sup>c</sup> | -1.492 <sup>c</sup>   | -1.865 <sup>c</sup> |
| <b>7J</b> | -2.991 <sup>c</sup> | -1.338 <sup>c</sup> | -1.745 <sup>c</sup>   | -0.382 <sup>b</sup> |
| <b>7K</b> | -2.571 <sup>c</sup> | -0.513 <sup>b</sup> | -1.668 <sup>c</sup>   | -0.722 <sup>b</sup> |
| <b>7L</b> | -3.075 <sup>c</sup> | -0.801 <sup>b</sup> | -1.674 <sup>c</sup>   | -0.468 <sup>b</sup> |
| <b>7M</b> | -3.831 <sup>c</sup> | -1.628 <sup>c</sup> | -1.778 <sup>c</sup>   | -1.246 <sup>c</sup> |
| <b>7N</b> | -2.235 <sup>c</sup> | -1.386 <sup>c</sup> | -1.725 <sup>c</sup>   | -0.521 <sup>b</sup> |
| <b>7P</b> | -2.067 <sup>c</sup> | -1.177 <sup>c</sup> | -1.701 <sup>c</sup>   | -0.258 <sup>b</sup> |
| <b>7Q</b> | -3.327 <sup>c</sup> | -0.692 <sup>b</sup> | -1.671 <sup>c</sup>   | -0.282 <sup>b</sup> |
| <b>7R</b> | -3.411 <sup>c</sup> | -0.481 <sup>b</sup> | -1.732 <sup>c</sup>   | -1.065 <sup>c</sup> |
| <b>8A</b> | -0.618 <sup>b</sup> | -1.949 <sup>c</sup> | -0.672 <sup>b</sup>   | 0.105 <sup>a</sup>  |
| <b>8B</b> | -0.786 <sup>b</sup> | -1.367 <sup>c</sup> | -0.625 <sup>b</sup>   | 0.108 <sup>a</sup>  |
| <b>8C</b> | -1.122 <sup>c</sup> | -1.266 <sup>c</sup> | -0.628 <sup>b</sup>   | 0.442 <sup>a</sup>  |
| <b>8D</b> | -2.466 <sup>c</sup> | -1.428 <sup>c</sup> | -0.684 <sup>b</sup>   | -0.818 <sup>b</sup> |
| <b>8E</b> | -0.114 <sup>b</sup> | -1.659 <sup>c</sup> | -0.642 <sup>b</sup>   | 0.089 <sup>a</sup>  |
| <b>8F</b> | -0.786 <sup>b</sup> | -0.999 <sup>b</sup> | -0.658 <sup>b</sup>   | 0.498 <sup>a</sup>  |
| <b>8G</b> | -0.786 <sup>b</sup> | -0.970 <sup>b</sup> | -0.618 <sup>b,d</sup> | 0.760 <sup>a</sup>  |

<sup>a</sup> Highly active compound. <sup>b</sup> Moderately active compound. <sup>c</sup> Weakly active to inactive compound. <sup>d</sup> The most potent compound against each cancer cell line. <sup>e</sup> Not tested. <sup>f</sup> Experimental pIC<sub>50</sub> values.

**Table S2** Predicted cytotoxic activity (pIC<sub>50</sub>) of modified compounds (**1A-1R**, **2A-2R**, **7A-7R** and **8A-8R**) and experimental cytotoxic activity of reference drugs (continue)

| Compound    | pIC <sub>50</sub>    |                     |                     |                      |
|-------------|----------------------|---------------------|---------------------|----------------------|
|             | HuCCA-1              | HepG2               | A549                | MOLT-3               |
| <b>8H</b>   | -0.702 <sup>b</sup>  | -0.574 <sup>b</sup> | -0.640 <sup>b</sup> | -0.333 <sup>b</sup>  |
| <b>8J</b>   | -1.038 <sup>c</sup>  | -1.789 <sup>c</sup> | -0.867 <sup>b</sup> | 0.177 <sup>a</sup>   |
| <b>8K</b>   | -1.122 <sup>c</sup>  | -1.139 <sup>c</sup> | -0.779 <sup>b</sup> | -0.204 <sup>b</sup>  |
| <b>8L</b>   | -0.366 <sup>b</sup>  | -1.391 <sup>c</sup> | -0.779 <sup>b</sup> | 0.110 <sup>a</sup>   |
| <b>8M</b>   | -0.618 <sup>b</sup>  | -1.571 <sup>c</sup> | -0.901 <sup>b</sup> | -0.485 <sup>b</sup>  |
| <b>8N</b>   | 0.054 <sup>a,d</sup> | -1.656 <sup>c</sup> | -0.851 <sup>b</sup> | 0.068 <sup>a</sup>   |
| <b>8P</b>   | -0.702 <sup>b</sup>  | -1.113 <sup>c</sup> | -0.815 <sup>b</sup> | 0.571 <sup>a</sup>   |
| <b>8Q</b>   | -1.038 <sup>c</sup>  | -1.285 <sup>c</sup> | -0.778 <sup>b</sup> | 0.947 <sup>a,d</sup> |
| <b>8R</b>   | -0.282 <sup>b</sup>  | -1.013 <sup>c</sup> | -0.859 <sup>b</sup> | -0.645 <sup>b</sup>  |
| Etoposide   | - <sup>e</sup>       | -1.479 <sup>f</sup> | - <sup>e</sup>      | 1.292 <sup>f</sup>   |
| Doxorubicin | 0.081 <sup>f</sup>   | 0.102 <sup>f</sup>  | 0.357 <sup>f</sup>  | - <sup>e</sup>       |

<sup>a</sup> Highly active compound. <sup>b</sup> Moderately active compound. <sup>c</sup> Weakly active to inactive compound. <sup>d</sup> The most potent compound against each cancer cell line. <sup>e</sup> Not tested. <sup>f</sup> Experimental pIC<sub>50</sub> values.