Task ID: 425.035

Task Title: High-Throughput Cellular-Based Toxicity Assays for Manufactured Nanoparticles and Nanostructure-Toxicity Relationships Models

Deliverable #4: Collect, curate, and assemble all data available from the literature, web resources, participating industry, collaborators.

Summary/Abstract:

This report summarizes our recent efforts on collecting and curating publicly available experimental data on toxicity related biological assays of nanoparticles. Our goal was to indentify data of sufficient size to enable statistical modeling. So far, we have collected and curated three independent datasets from three distinct research groups. Each dataset was either extracted from relevant publication or obtained directly from the authors, and formatted for subsequent descriptor calculation and computational modeling.

Technical Results and Data:

The following datasets were collected:

1) The first dataset included 51 diverse nanoparticles, which were evaluated at four different doses in four cell types, using four physiological assays (**Figure 1**) [1]. Particle features, such as size, zeta potential and relaxitivities, were also available for each nanoparticle in the dataset.
2) The second dataset consisted of 109 nanoparticles with the same core (CLIO, cross-linked iron oxide) but different modifiers attached to the surface of nanoparticles (**Figure 2**). [2]. These nanoparticles were tested against five different cell lines with regards to cellular uptake. The distribution of cellular uptake data suggested that specific surface modifications of nanoparticles could lead to a change in cellular uptake especially in PaCa2 cell line.
3) The third dataset included 84 nanoparticles with the same core (MWNT, multi-walled nanotube) but, again, with different surface modifiers (**Figure 3**) [3]. These nanoparticles were tested against six endpoints including protein binding (BSA, carbonic anhydrase, chymotrypsin and hemoglobin), acute toxicity and immune toxicity.

For all three datasets we have collected and formatted available data to enable subsequent descriptor calculation and modeling building.

A

MNP	CLIO	PNP	MION	QD	Feridex IV	Ferrum Hausmann
# particle	23	19	4	3	1	1

B

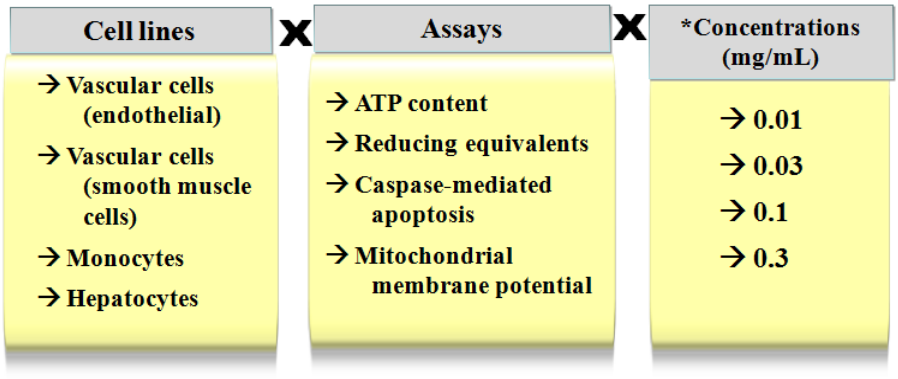
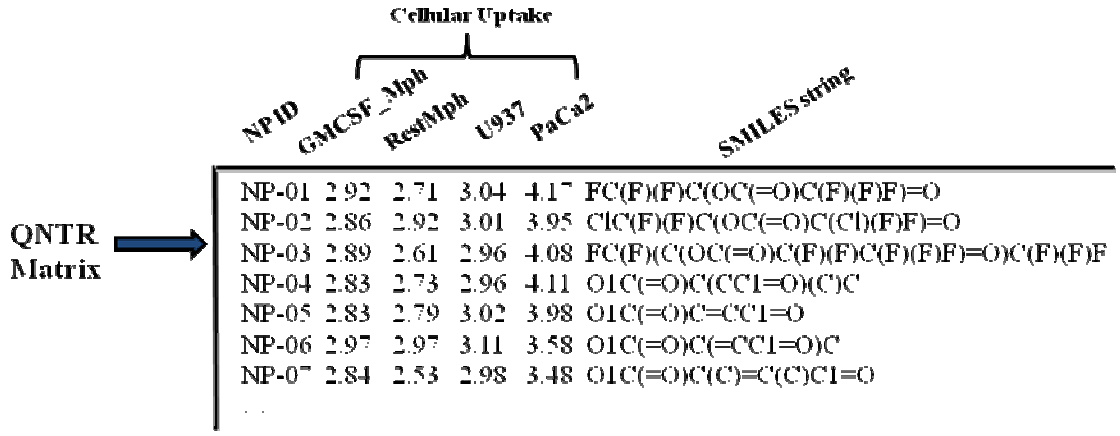


Figure 1. The description of the first dataset. 51 nanoparticles with diverse structures (A) were tested against 4 cell lines at 4 different concentrations using 4 physiological assays (B). *For quantum dots, the tested concentration are 3, 10, 30, and 100 nM.

A



B

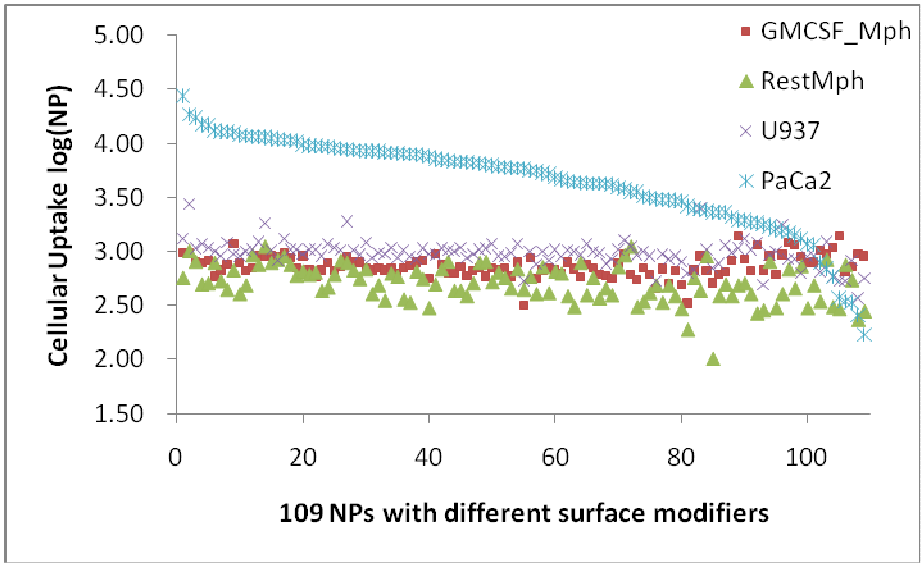
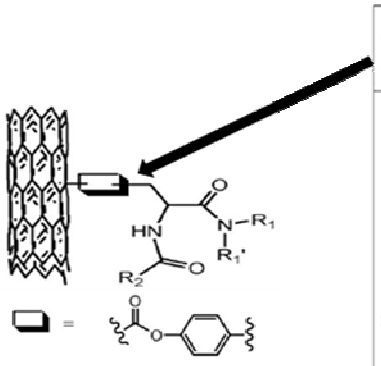


Figure 2. Summary of data for the second dataset of 109 nanoparticles with the same core but different surface modifiers. Each NP was represented by the structure of the surface-attached molecule using SMILES strings (A). Distribution of cellular uptake in four different cell lines is shown as well (B).



		$R_1R_1'N$-							
		AM001	AM002	AM003	AM004	AM005	AM006	AM007	AM008
R2-	Fmoc	5	6	7	8	9	10	11	12
	De-Fmoc	13	14	15	16	17	18	19	20
	AC001	21	29	37	45	53	61	69	77
	AC002	22	30	38	46	54	62	70	78
	AC003	23	31	39	47	55	63	71	79
	AC004	24	32	40	48	56	64	72	80
	AC005	25	33	41	49	57	65	73	81
	AC006	26	34	42	50	58	66	74	82
	AC007	27	35	43	51	59	67	75	83
	AC008	28	36	44	52	60	68	76	84

Figure 3. Data summary for the third dataset with 84 nanoparticles. Like the second dataset, each nanoparticle was represented by its surface molecule. The surface modifiers differed only in R1, R1' and R2 positions.

References:

1. Shaw, S.Y., et al., *Perturbational profiling of nanomaterial biologic activity.* Proc Natl Acad Sci U S A, 2008. **105**(21): p. 7387-92.
2. Weissleder, R., et al., *Cell-specific targeting of nanoparticles by multivalent attachment of small molecules.* Nat Biotechnol, 2005. **23**(11): p. 1418-23.
3. Zhou, H., et al., *A nano-combinatorial library strategy for the discovery of nanotubes with reduced protein-binding, cytotoxicity, and immune response.* Nano Lett, 2008. **8**(3): p. 859-65.