**Imidazolium-based Zwitterionic liquid-modified PEG-PLGA nanoparticles as a potential intravenous drug delivery carrier.**

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**Supporting Information**

**EO2ImBS (ZIL-1)**

A black and white image of a molecule

Description automatically generated

1H NMR (400 MHz, D2O) δ 8.79 (s, 1H), 7.49 (t, *J* = 1.6 Hz, 2H), 4.34 (t, *J* = 4.9 Hz, 2H), 4.21 (t, *J* = 7.1 Hz, 2H), 3.85 (t, *J* = 4.9 Hz, 2H), 3.62 (dd, *J* = 5.6, 2.9 Hz, 2H), 3.56 – 3.49 (m, 2H), 3.29 (s, 3H), 2.88 (t, *J* = 7.7 Hz, 2H), 1.98 (p, *J* = 7.3 Hz, 2H), 1.75 – 1.63 (m, 2H).

**EO2ImPS (ZIL-2)**

A black and white image of a molecule

Description automatically generated

1H NMR (400 MHz, D2O) δ 8.80 (d, *J* = 1.8 Hz, 1H), 7.51 (q, *J* = 1.9 Hz, 2H), 4.41 – 4.28 (m, 4H), 3.90 – 3.81 (m, 2H), 3.68 – 3.59 (m, 2H), 3.59 – 3.49 (m, 2H), 3.29 (s, 3H), 2.86 (dd, *J* = 8.2, 6.5 Hz, 2H), 2.27 (p, *J* = 7.2 Hz, 2H).

**EO3ImPS (ZIL-3)**

A black and white drawing of a chemical structure

Description automatically generated

1H NMR (400 MHz, D2O) δ 8.80 (d, *J* = 1.7 Hz, 1H), 7.50 (d, *J* = 1.6 Hz, 2H), 4.38 – 4.28 (m, 4H), 3.89 – 3.81 (m, 2H), 3.66 – 3.56 (m, 7H), 3.56 – 3.49 (m, 2H), 3.30 (s, 3H), 2.85 (dd, *J* = 8.2, 6.5 Hz, 2H), 2.26 (p, *J* = 7.2 Hz, 2H).

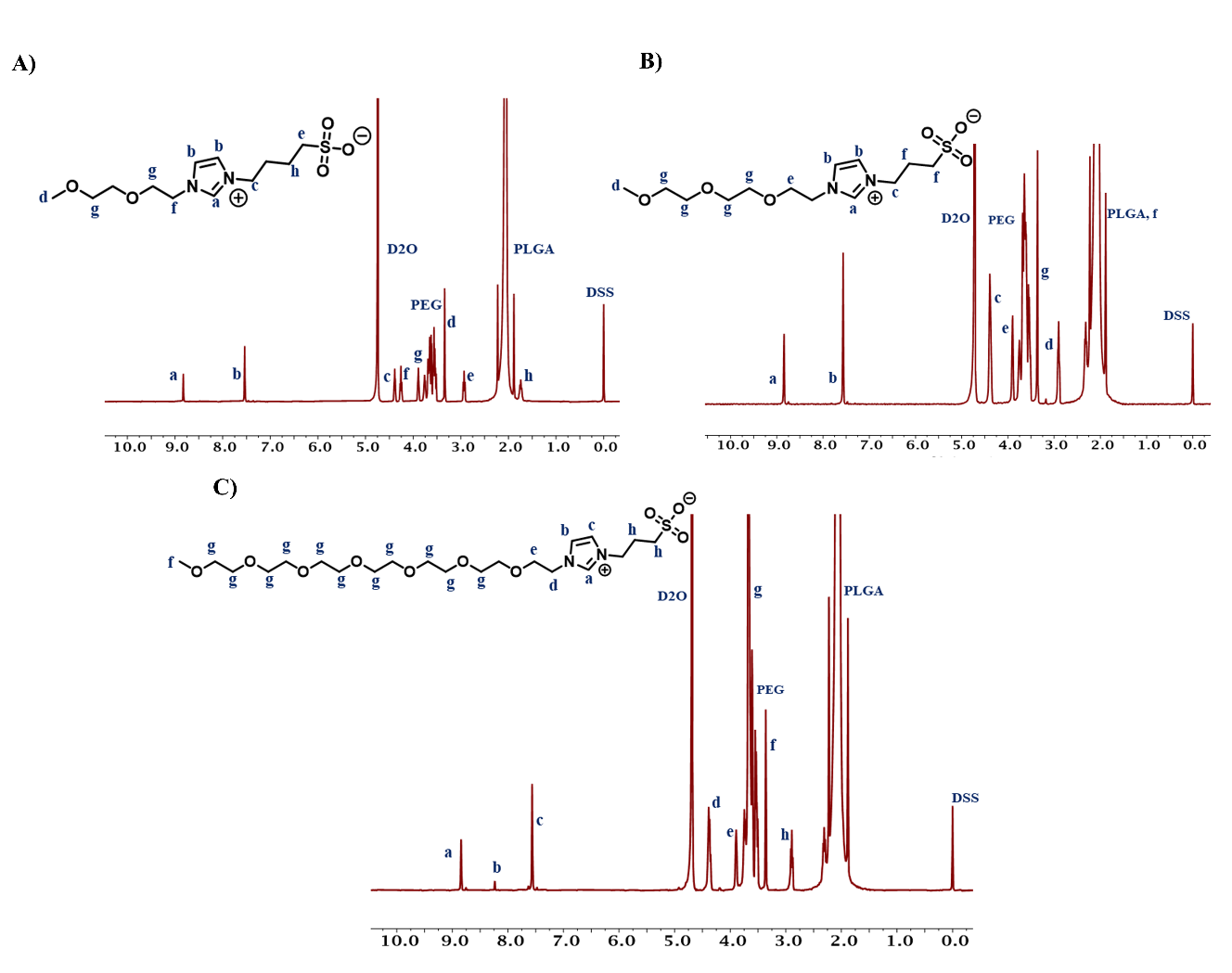
**EO7ImPS (ZIL-4)**

A black and white drawing of a molecule

Description automatically generated

1H NMR (400 MHz, D2O) δ 8.81 (s, 0H), 7.54 – 7.48 (m, 1H), 4.40 – 4.28 (m, 2H), 3.85 (td, *J* = 4.6, 2.2 Hz, 1H), 3.61 (d, *J* = 8.0 Hz, 11H), 3.30 (s, 1H), 2.86 (q, *J* = 7.6 Hz, 1H), 2.26 (p, *J* = 7.2 Hz, 1H).

**Figure S1. Ionic liquid 1H NMR characterization.**



**Chemical shift (ppm)**

**Chemical shift (ppm)**

**Chemical shift (ppm)**

**Figure S2. 1H NMR spectrum for ZIL coated PEG-PLGA nanoparticles**. (A) PEG-PLGA-NP-ZIL-1, (B) PEG-PLGA-NP-ZIL-3, (C) PEG-PLGA-NP-ZIL-4.

A table with numbers and letters

Description automatically generatedA diagram of a graph

Description automatically generated with medium confidence

**Figure S3. 1H NMR spectrum shifts for neat ZIL vs. ZIL coated PEG-PLGA nanoparticles**. (A) PEG-PLGA-NP-ZIL-1, (B) PEG-PLGA-NP-ZIL-2, (C) PEG-PLGA-NP-ZIL-3, (D) PEG-PLGA-NP-ZIL-4. (E) The amount of each ionic liquid coating per nanoparticle sample (1 mg/mL) via 1H NMR spectroscopic analysis (n =3, mean ± SD).

A group of graphs with numbers

Description automatically generated

A graph of different sizes and numbers

Description automatically generated with medium confidence

**Figure S4. PEG-PLGA NP and ZIL-NP DLS stability profile,** size (nm), PDI, and zeta potential (mv) with time (A-E) PEG-PLGA, ZIL-1-NP, ZIL-2-NP, ZIL-3-NP, and ZIL-4-NP respectively. (n =3, mean ±SD).

A graph of different numbers and numbers

Description automatically generated with medium confidence

**Figure S5. PEG-PLGA NP and ZIL-NP DID release with time** show minimum release profile within 48 h. at 37°C, pH 7.4 in 1x PBS buffer **(**n=3, mean ± SD).

**1.1. Coagulation and Hemostasis Proteins: 4**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P00734 | Prothrombin | -0.100 | -0.334 | -0.180 | -0.141 | -0.455 |
| P01008 | Antithrombin-III | 0.013 | -0.458 | -0.310 | -0.264 | -0.475 |
| P00747 | Plasminogen | -0.094 | -0.530 | -0.396 | -0.349 | -0.431 |
| P01042 | Kininogen-1 | -0.236 | -0.713 | -0.448 | -0.436 | -0.549 |

**1.2. Coagulation and Hemostasis Proteins: 3**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P19221 | Prothrombin | -0.017 | 0.303 | 0.477 | 0.365 | 0.406 |
| Q3U3V1 | Coagulation factor X | 0.145 | 0.378 | 0.546 | 0.430 | 0.625 |
| P20918 | Plasminogen | 0.079 | 0.372 | 0.473 | 0.418 | 0.410 |

**2.1. Immunoglobulins and Immune-Related Proteins: 10**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| A0A0G2JMB2 | Immunoglobulin heavy constant alpha2 (Fragment) | 0.968 | -0.411 | 0.403 | 0.231 | 0.238 |
| P0DOY2 | Immunoglobulin lambda constant 2 | 0.334 | -0.686 | -0.562 | -0.259 | -0.119 |
| P01591 | Immunoglobulin J chain | 0.824 | -0.692 | -0.313 | -0.205 | -0.285 |
| P01861 | Immunoglobulin heavy constant gamma 4 | -0.421 | -0.698 | -0.558 | -0.447 | -0.721 |
| P01859 | Immunoglobulin heavy constant gamma 2 | 0.388 | -0.242 | -0.500 | -0.094 | -0.258 |
| P01860 | Immunoglobulin heavy constant gamma 3 | -0.577 | -1.013 | -0.505 | -0.862 | -0.859 |
| P01871 | Immunoglobulin heavy constant mu | 0.276 | -0.451 | -0.288 | -0.090 | -0.291 |
| P01876 | Immunoglobulin heavy constant alpha 1 | -0.008 | -0.627 | -0.417 | -0.497 | -0.597 |
| P01857 | Immunoglobulin heavy constant gamma 1 | 0.008 | -0.532 | -0.389 | -0.327 | -0.389 |
| P01834 | Immunoglobulin kappa constant | 0.045 | -0.673 | -0.498 | -0.433 | -0.434 |

**2.2. Immunoglobulins and Immune-Related Proteins: 20**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| A0A140T8P3 | Immunoglobulin kappa chain variable 15-103(Fragment) | -0.035 | 1.302 | 1.383 | 1.285 | 0.479 |
| A0A140T8P3 | Immunoglobulin kappa variable 4-53 | 0.137 | 0.432 | 0.605 | 0.535 | 0.542 |
| A0A075B5M7 | Immunoglobulin kappa variable 5-39 | -0.098 | 0.350 | 0.524 | 0.436 | 0.383 |
| A0A0B4J1P4 | Immunoglobulin heavy variable 5-16(Fragment) | -0.404 | 0.031 | -0.036 | -0.107 | 0.085 |
| A0A075B5K2 | Immunoglobulin kappa chain variable 9-124 | -0.035 | 0.559 | 0.757 | 0.615 | 0.664 |
| A0A140T8P6 | Immunoglobulin kappa variable 12-46(Fragment) | 0.042 | 0.344 | 0.437 | 0.325 | 0.507 |
| P01592 | Immunoglobulin J chain | -0.140 | 0.240 | 0.342 | 0.293 | 0.413 |
| A0A0B4J1H7 | Immunoglobulin kappa variable 1-135(Fragment) | 0.029 | 0.282 | 0.373 | 0.264 | 0.407 |
| F6TQW2 | Immunoglobulin heavy constant gamma 2C(Fragment) | 0.051 | 0.646 | 0.720 | 0.639 | 0.572 |
| P01837 | Immunoglobulin kappa constant | 0.133 | 0.322 | 0.509 | 0.409 | 0.539 |
| A0A075B5V6 | Immunoglobulin heavy variable V1-42 | -0.063 | 0.214 | 0.413 | 0.326 | 0.356 |
| P01837 | Immunoglobulin heavy constant alpha 1 | 0.047 | 0.358 | -0.012 | -0.107 | 0.440 |
| A0A075B5P5 | Immunoglobulin heavy constant gamma 3(Fragment) | 0.033 | 0.429 | 0.470 | 0.400 | 0.559 |
| A0A075B5P3 | Immunoglobulin heavy constant gamma 2B(Fragment) | 0.100 | 0.047 | 0.214 | 0.139 | 0.605 |
| A0A075B5P6 | Immunoglobulin heavy constant mu (Fragment) | -0.027 | 0.441 | 0.515 | 0.409 | 0.495 |
| P01878 | Ig alpha chain C region | -0.084 | 0.377 | 1.293 | 1.150 | 0.399 |
| P01843 | Ig lambda-1chain C | 0.258 | 0.681 | 0.741 | 0.672 | 0.665 |
| P01863 | Ig gamma-2A chain C region, A allele | -0.047 | 0.289 | 0.336 | 0.318 | 0.481 |
| P01644 | Ig kappa chain V-V region HP | -0.285 | 0.320 | 0.363 | 0.287 | 0.309 |
| A0A075B5P4 | Ig gamma-1 chain C region secreted form (Fragment) | 0.109 | 0.259 | 0.387 | 0.308 | 0.414 |

**3.1. Lipid and Lipoprotein: 9**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P05090 | Apolipoprotein D | 0.297 | -0.544 | -0.277 | -0.192 | -0.298 |
| P02656 | Apolipoprotein C-III | 0.041 | -0.358 | -0.260 | -0.159 | -0.431 |
| P02652 | Apolipoprotein A-II | 0.064 | -0.696 | -0.477 | -0.297 | -0.394 |
| O14791 | Apolipoprotein L1 | -0.218 | -0.802 | -0.510 | -0.425 | -0.514 |
| P08519 | Apolipoprotein(a) | 0.977 | 0.831 | 0.577 | 0.909 | 0.541 |
| P02649 | Apolipoprotein E | 0.607 | 0.224 | 0.045 | 0.409 | 0.247 |
| P06727 | Apolipoprotein A-IV | -0.378 | -0.916 | -0.715 | -0.495 | -0.952 |
| P02647 | Apolipoprotein A-I | 0.052 | -0.665 | -0.425 | -0.313 | -0.418 |
| P04114 | Apolipoprotein B-100 | 0.589 | 0.214 | 0.158 | 0.403 | 0.174 |

**3.2. Lipid and Lipoprotein: 4**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| Q00623 | Apolipoprotein A-I | -0.007 | 0.303 | 0.382 | 0.290 | 0.402 |
| P09813 | Apolipoprotein A-II | 0.034 | 0.285 | 0.441 | 0.352 | 0.531 |
| P08226 | Apolipoprotein E | -0.020 | 0.307 | 0.408 | 0.303 | 0.420 |
| P06728 | Apolipoprotein A-IV | -0.028 | 0.302 | 0.459 | 0.360 | 0.448 |

**4.1. Glycoproteins: 7**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P02750 | Leucine-rich alpha-2-glycoprotein | 0.162 | -0.499 | -0.312 | -0.123 | -0.224 |
| P25311 | Zinc-alpha-2-glycoprotein | -0.295 | -0.623 | -0.352 | -0.450 | -0.962 |
| P02749 | Beta-2-glycoprotein 1 | -0.055 | -0.367 | -0.344 | -0.082 | -0.701 |
| P02765 | Alpha-2-HS-glycoprotein | 0.272 | -0.302 | -0.192 | -0.181 | -0.272 |
| P02763 | Alpha-1-acid glycoprotein 1 | -0.210 | -0.455 | -0.386 | -0.183 | -0.647 |
| P04217 | Alpha-1B-glycoprotein | -0.295 | -0.834 | -0.612 | -0.615 | -0.823 |
| P27169 | Serum paraoxonase/arylesterase 1 | -0.057 | -0.497 | -0.276 | -0.302 | -0.312 |

**4.2. Glycoproteins: 6**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| Q91XL1 | Leucine-rich HEV glycoprotein | -0.125 | 0.176 | 0.171 | 0.156 | 0.220 |
| Q64726 | Zinc-alpha-2-glycoprotein | 0.299 | 0.300 | 0.490 | 0.438 | 0.451 |
| A0A0R4J039 | Histidine-rich glycoprotein | -0.012 | 0.403 | 0.425 | 0.383 | 0.480 |
| P29699 | Alpha-2-HS-glycoprotein | 0.193 | 0.489 | 0.478 | 0.351 | 0.499 |
| Q01339 | Beta-2-glycoprotein1 | 0.041 | 0.310 | 0.474 | 0.315 | 0.388 |
| P35441 | Thrombospondin-1 | 0.021 | 0.211 | 0.261 | 0.206 | 0.307 |

**5.1. Protease Inhibitors and Enzymes: 8**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P01009 | Alpha-1-antitrypsin | -1.187 | -1.686 | -0.371 | -0.235 | -0.354 |
| P01011 | Alpha-1-antichymotrypsin | 0.031 | -0.601 | -0.327 | -0.230 | -0.420 |
| P19827 | Inter-alpha-trypsin inhibitor heavy chain H1 | -0.398 | -0.716 | -0.507 | -0.515 | -0.800 |
| P19823 | Inter-alpha-trypsin inhibitor heavy chain H2 | -0.099 | -0.557 | -0.403 | -0.220 | -0.492 |
| P00761 | Trypsin | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| P05155 | Plasma protease C1 inhibitor | -0.057 | -0.483 | -0.296 | -0.282 | -0.477 |
| P01023 | Alpha-2-macroglobulin | -0.064 | -0.539 | -0.380 | -0.269 | -0.465 |
| P02760 | Protein AMBP | -0.396 | -0.704 | -0.374 | -0.484 | -0.665 |

**5.2. Protease Inhibitors and Enzymes: 18**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P07759 | Serine protease inhibitor A3N | 0.089 | 0.232 | 0.295 | 0.435 | 0.406 |
| Q91WP6 | Serine protease inhibitor A3K | -0.025 | 0.262 | 0.326 | 0.247 | 0.369 |
| P32261 | Antithrombin-III | -0.026 | 0.508 | 0.412 | 0.409 | 0.387 |
| Q9QXC1 | Fetuin-B | -0.051 | 0.279 | 0.294 | 0.255 | 0.294 |
| Q9QWK4 | CD5 antigen-like | 0.147 | 0.289 | 0.399 | 0.310 | 0.375 |
| Q9DBD0 | Inhibitor of carbonic anhydrase | 0.000 | 0.360 | 0.419 | 0.362 | 0.378 |
| Q61704 | Inter-alpha-trypsin inhibitor heavy chain H3 | -0.280 | 0.140 | 0.175 | 0.102 | 0.250 |
| P22599 | Alpha-1-antitrypsin1-2 | 0.026 | -0.439 | -0.348 | -0.397 | -0.357 |
| P28665 | Murinoglobulin-1 | 0.020 | 0.326 | 0.397 | 0.358 | 0.422 |
| P28666 | Murinoglobulin-2 | -0.003 | 0.462 | 0.537 | 0.471 | 0.546 |
| Q61838 | Pregnancy zone protein | 0.002 | 0.352 | 0.408 | 0.345 | 0.440 |
| P00761 | Trypsin | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| P26262 | Plasma kallikrein | 0.176 | 0.253 | 0.353 | 0.212 | 0.328 |
| Q8VCU2 | Glycosyl-phosphatidylinositol-specific phospholipase D | 0.106 | 0.094 | 0.407 | 0.302 | 0.332 |
| P23953 | Carboxy lesterase1C | 0.000 | 0.285 | 0.349 | 0.270 | 0.316 |
| Q9JJN5 | Carboxy peptidase N catalytic chain | 0.263 | 0.249 | 0.270 | 0.278 | 0.455 |
| Q9DBB9 | Carboxy peptidase N subunit 2 | 0.021 | 0.605 | 0.643 | 0.602 | 0.635 |
| G3X977 | Inter-alpha-trypsin inhibitor heavy chain H2 | -0.050 | 0.407 | 0.484 | 0.384 | 0.510 |

**6.1. Complement Proteins: 4**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P01031 | Complement C5 | -0.010 | -0.734 | -0.342 | -0.022 | -0.483 |
| P08603 | Complement factor H | -0.100 | -0.596 | -0.415 | -0.284 | -0.508 |
| B4E1Z4 | Complement factor | 0.086 | -0.594 | -0.247 | -0.281 | -0.434 |
| P01024 | Complement C3 | 0.026 | -0.502 | -0.353 | -0.210 | -0.411 |

**6.2. Complement Proteins: 5**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| B8JJN0 | Complement C2 | 0.104 | 0.368 | 0.455 | 0.348 | 0.453 |
| E9Q8I0 | Complement factor H | 0.059 | 0.418 | 0.531 | 0.431 | 0.549 |
| P01029 | ComplementC4-B | 0.162 | 0.366 | 0.429 | 0.339 | 0.463 |
| P01027 | ComplementC3 | -0.005 | 0.307 | 0.383 | 0.317 | 0.422 |
| Q61129 | Complement factor I | -0.029 | 0.376 | 0.401 | 0.348 | 0.484 |

**7.1. Hemoglobin and Iron Metabolism Proteins: 4**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P05546 | Heparin cofactor 2 | 0.084 | -0.692 | -0.392 | -0.219 | -0.405 |
| P00450 | Ceruloplasmin | 0.005 | -0.493 | -0.309 | -0.306 | -0.402 |
| P02787 | Serotransferrin | 0.015 | -0.421 | -0.331 | -0.196 | -0.408 |
| P00738 | Haptoglobin | 0.027 | -0.442 | -0.280 | -0.135 | -0.347 |

**7.2**. **Hemoglobin and Iron Metabolism Proteins: 2**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| A8DUK4 | Beta-globin | 0.049 | 0.309 | 0.352 | 0.288 | 0.330 |
| Q61646 | Haptoglobin | 0.032 | 0.416 | 0.524 | 0.441 | 0.586 |

**8.1.** **Transport and Binding Proteins: 6**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P02768 | Albumin | 0.044 | -0.532 | -0.436 | -0.283 | -0.433 |
| P02774 | Vitamin D-binding protein | 0.037 | -0.438 | -0.276 | -0.175 | -0.400 |
| P43652 | Afamin | -0.050 | -0.596 | -0.439 | -0.283 | -0.485 |
| P02790 | Hemopexin | -0.063 | -0.569 | -0.388 | -0.361 | -0.607 |
| P00450 | Ceruloplasmin | 0.005 | -0.493 | -0.309 | -0.306 | -0.402 |
| P04003 | C4b-binding protein alpha chain | 0.091 | -0.447 | -0.306 | -0.026 | -0.262 |

**8.2.** **Transport and Binding Proteins: 11**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P01898 | H-2 class I histocompatibility antigen, Q10 alpha chain | 0.085 | 0.316 | 0.368 | 0.294 | 0.363 |
| Q06770 | Corticosteroid-binding globulin | 0.041 | 0.410 | 0.436 | 0.311 | 0.323 |
| P29788 | Vitronectin | 0.068 | 0.700 | 0.737 | 0.763 | 0.880 |
| P21614 | Vitamin D-binding protein | 0.034 | 0.545 | 0.547 | 0.475 | 0.537 |
| O89020 | Afamin | -0.024 | 0.355 | 0.408 | 0.362 | 0.483 |
| Q91X72 | Hemopexin | 0.070 | 0.244 | 0.345 | 0.224 | 0.333 |
| Q921I1 | Serotransferrin | 0.012 | 0.345 | 0.411 | 0.322 | 0.450 |
| P07724 | Albumin | 0.049 | 0.375 | 0.423 | 0.352 | 0.421 |
| Q3UHL6 | Fibronectin | 0.070 | 0.372 | 0.484 | 0.379 | 0.410 |
| P13020 | Gelsolin | 0.009 | 0.309 | 0.357 | 0.288 | 0.363 |
| P12246 | Serum amyloid P-component | 0.073 | 0.329 | 0.536 | 0.391 | 0.500 |

**9.1.** **Regulatory and Regulatory-Like Proteins: 3**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P01019 | Angiotensinogen | 0.241 | -0.341 | -0.192 | 0.163 | -0.155 |
| P00739 | Haptoglobin-related protein | 0.040 | -0.200 | 0.099 | 0.074 | -0.027 |
| P10909 | Clusterin | -0.038 | -0.529 | -0.316 | -0.240 | -0.440 |

**9.2.** **Regulatory and Regulatory-Like Proteins: 3**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **UniProtID** | **Protein Name** | **PEG-PLGA** | **ZIL-1-NP** | **ZIL-2-NP** | **ZIL-3-NP** | **ZIL-4-NP** |
| P63260 | Actin, cytoplasmic 2 | -0.159 | 0.281 | 0.386 | 0.253 | 0.302 |
| Q06890 | Clusterin | -0.056 | 0.170 | 0.323 | 0.169 | 0.293 |
| A0A0R4J038 | Bradykinin | -0.034 | 0.313 | 0.441 | 0.334 | 0.474 |

**Figure S6. LC-MS/MS analysis of NP hard protein corona shows relative adsorption and depletion of various human and mouse serum proteins depending on the ZIL used in a heatmap.** Proteins are categorized into 9 categories based on their primary known functions and color-coded orange for humans and green for mice. Proteins that are common to both species are shaded in gray. The intensity of the trypsin (used for digestion of samples) was used to normalize the relative abundance of serum proteins absorbed onto the nanoparticle surface PEG-PLGA and ZIL-coated PEG-PLGA particles; the final values represented log10.

A group of graphs showing different types of probiotics

Description automatically generated

A graph of lipid and lipoproteins

Description automatically generated

A graph of different colored lines

Description automatically generated

**Figure S7. A relative abundance of common proteins found in both human and mouse NP hard protein corona was categorized based on primary known functions.** Pattern-filled bars represent the abundance of mouse serum proteins in respect to the human serum protein represented by the solid color bar.