

**Supplementary Figure 1.** Impact of HLE strategies used for Factor IX on the volume of distribution of drugs present in the entire dataset.

| **Molecule** | **Strategy** | **MW (Da)** | **Delta MW (Da)** | **HLE MW (Da)** | **Species** | **Half-Life (h)** | **HLE Half-Life (h)** | **CL (mL/h/kg)** | **HLE CL (mL/h/kg)** | **Vss (mL/kg)** | **HLE Vss (mL/kg)** | **Reference** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| (Fab)2 | PEG | 100000 | 20000 | 120000 | Mouse | 7.06 | 11.5 | 13.9 | 9.71 | 132 | 213 | (Kitamura et al., 1990) |
| (Fab)2 | PEG (Branched) | 100000 | 40000 | 140000 | Rabbit | 7.72 | 45.0 | 14.3 | 1.09 | 59.8 | 49.6 | (Koumenis et al., 2000) |
| (Fab)2 | PEG (Branched) | 100000 | 80000 | 180000 | Rabbit | 7.72 | 51.2 | 14.3 | 0.728 | 59.8 | 52.2 | (Koumenis et al., 2000) |
| Α1-Antitrypsin | Polysialic Acid | 52000 | 20000 | 72000 | Mouse | 15.1 | 27.8 | 732 | 72.0 | 13201 | 2714 | (Lindhout et al., 2011) |
| Adnectin C | PAS-200 | 11374 | 16703 | 28077 | Mouse | 1.42 | 5.96 | 74.7 | 10.0 | 152 | 62.1 | (Aghaabdollahian et al., 2019) |
| Adrenomedullin | PEG | 6029 | 5000 | 11029 | Rat | 0.126 | 0.983 | 98544 | 16906 | 10499 | 18990 | (Kubo et al., 2014) |
| Alpha-Momorcharin | PEG | 28585 | 30000 | 58585 | Rat | 0.261 | 3.89 | 3151 | 62.4 | 664 | 136 | (Deng et al., 2016) |
| BDD Factor VIII | Fc Fusion, Human IgG1 | 167000 | 50000 | 217000 | Dog | 9.07 | 19.4 | 7.09 | 4.91 | 75.3 | 96.0 | (Dumont et al., 2012) |
| BDD Factor VIII | Fc Fusion, Human IgG1 | 167000 | 50000 | 217000 | Human | 19.8 | 93.0 | 3.50 | 2.13 | 63.5 | 89.6 | (Powell et al., 2012) |
| BDD Factor VIII | Fc Fusion, Human IgG1 | 167000 | 50000 | 217000 | Mouse | 7.18 | 14.7 | 4.83 | 3.81 | 57.2 | 68.3 | (Dumont et al., 2012) |
| BDD Factor VIII | PEG | 167000 | 40000 | 207000 | Dog | 16.2 | 19.2 | 6.56 | 3.87 | 73.8 | 72.4 | (Agerso et al., 2012) |
| BDD Factor VIII | PEG | 167000 | 60000 | 227000 | Human | 12.5 | 17.6 | 2.37 | 1.56 | 39.6 | 36.8 | (Coyle et al., 2014) |
| BIO5192 | PEG | 818 | 20000 | 20818 | Rat | 1.06 | 18.6 | 635 | 6.28 | 188 | 86.1 | (Pepinsky et al., 2005) |
| Carboxypeptidase A | PEG | 35000 | 5000 | 40000 | Rat | 12.7 | 12.3 | 38.4 | 29.5 | 316 | 217 | (Ton et al., 2005) |
| Carboxypeptidase A | PEG | 35000 | 10000 | 45000 | Rat | 12.7 | 9.89 | 38.4 | 13.1 | 316 | 98.8 | (Ton et al., 2005) |
| Carboxypeptidase A | PEG | 35000 | 15000 | 50000 | Rat | 12.7 | 10.7 | 38.4 | 6.96 | 316 | 71.8 | (Ton et al., 2005) |
| CD44-3MUT | PEG | 11500 | 20000 | 31500 | Mouse | 0.205 | 11.0 | 260 | 2.60 | 42.0 | 41.0 | (Pink et al., 2014) |
| CNTF | Albumin Binding | 22900 | 5000 | 27900 | Rat | 0.694 | 19.3 | 341459 | 20323 | 366258 | 480298 | (Xu et al., 2017) |
| CNTF | PEG | 22900 | 20000 | 42900 | Rat | 0.694 | 14.6 | 341459 | 32003 | 366258 | 528782 | (Xu et al., 2017) |
| CNTF | PEG | 22900 | 40000 | 62900 | Rat | 0.694 | 17.5 | 341459 | 17071 | 366258 | 374302 | (Xu et al., 2017) |
| Cocaine Esterase | PEG | 130000 | 80000 | 210000 | Rat | 0.106 | 4.17 | 106 | 7.50 | 32.2 | 42.6 | (Huang et al., 2019) |
| Cocaine Hydrolase | Fc Fusion, Human IgG1 | 70000 | 100000 | 240000 | Rat | 8.16 | 140 | 23.8 | 0.273 | 98.7 | 41.1 | (Zheng et al., 2022) |
| Cytochrome c | Albumin Binding | 12000 | 1600 | 13600 | Rat | 0.112 | 0.933 | 787 | 24.8 | 121 | 33.9 | (Kunitomo et al., 1992) |
| DARPin | PAS-300 | 19300 | 25620 | 44920 | Mouse | 22.7 | 10.5 | 245 | 14.9 | 7821 | 165 | (Brandl et al., 2019) |
| DARPin | PAS-600 | 19300 | 50190 | 69490 | Mouse | 22.7 | 14.1 | 245 | 7.26 | 7821 | 133 | (Brandl et al., 2019) |
| DARPin | PAS-900 | 19300 | 74750 | 94050 | Mouse | 22.7 | 18.4 | 245 | 4.46 | 7821 | 113 | (Brandl et al., 2019) |
| DARPin | XTEN-288 | 19300 | 27630 | 46930 | Mouse | 22.7 | 10.4 | 245 | 14.1 | 7821 | 174 | (Brandl et al., 2019) |
| DARPin | XTEN-576 | 19300 | 53910 | 73210 | Mouse | 22.7 | 13.7 | 245 | 7.39 | 7821 | 131 | (Brandl et al., 2019) |
| DARPin | XTEN-864 | 19300 | 80330 | 99630 | Mouse | 22.7 | 20.6 | 245 | 4.01 | 7821 | 115 | (Brandl et al., 2019) |
| DARPin-Exotoxin A | PEG | 58700 | 20000 | 78700 | Mouse | 0.155 | 0.781 | 446 | 62.5 | 74.9 | 65.0 | (Simon et al., 2014) |
| Diabody | Albumin Binding | 52000 | 5000 | 57000 | Mouse | 0.679 | 53.3 | 812 | 1.37 | 354 | 86.1 | (Kenanova et al., 2010) |
| Diabody | Albumin Domain III, Human (Fusion) | 55000 | 46000 | 101000 | Mouse | 27.0 | 41.3 | 62.1 | 5.67 | 1948 | 312 | (Kenanova et al., 2010) |
| Diabody | PEG | 52500 | 7500 | 60000 | Mouse | 5.40 | 17.9 | 24.4 | 12.6 | 123 | 216 | (Li et al., 2011) |
| Diabody | PEG | 52000 | 10000 | 62000 | Mouse | 0.587 | 6.42 | 652 | 44.5 | 301 | 200 | (Li et al., 2018) |
| Diabody | PEG | 52500 | 17500 | 70000 | Mouse | 5.40 | 12.3 | 24.4 | 10.0 | 123 | 162 | (Li et al., 2011) |
| Diabody | PEG | 52000 | 20000 | 72000 | Mouse | 0.587 | 13.5 | 652 | 3.78 | 301 | 56.2 | (Li et al., 2018) |
| Diabody | PEG | 52500 | 27500 | 80000 | Mouse | 5.40 | 12.1 | 24.4 | 5.33 | 123 | 94.6 | (Li et al., 2011) |
| Diabody | PEG | 52000 | 40000 | 92000 | Mouse | 0.587 | 26.6 | 652 | 2.48 | 301 | 93.9 | (Li et al., 2018) |
| Diabody | PEG (Branched) | 52000 | 10000 | 62000 | Mouse | 0.587 | 4.88 | 652 | 17.1 | 301 | 79.6 | (Li et al., 2018) |
| Diabody | PEG (Branched) | 52000 | 20000 | 72000 | Mouse | 0.679 | 40.0 | 812 | 1.88 | 354 | 76.6 | (Kenanova et al., 2010) |
| Diabody | PEG (Branched) | 52000 | 40000 | 92000 | Mouse | 0.587 | 41.1 | 652 | 1.82 | 301 | 70.9 | (Li et al., 2018) |
| Diabody | PEG (Branched) | 52000 | 80000 | 132000 | Mouse | 0.587 | 42.1 | 652 | 1.35 | 301 | 73.3 | (Li et al., 2018) |
| Doxorubicin | PEG | 434 | 2221 | 2655 | Rat | 2.92 | 9.61 | 19393 | 833 | 62557 | 10058 | (Cao and Feng, 2008) |
| Endostatin | PEG | 20000 | 2000 | 22000 | Monkey | 12.7 | 24.7 | 491 | 171 | 6113 | 2683 | (Guo et al., 2019) |
| Erythropoietin | PEG | 35000 | 30000 | 65000 | Rat | 7.28 | 35.1 | 2.03 | 0.431 | 8.52 | 20.0 | (Cohan et al., 2011) |
| Exenatide | PEG | 4186 | 5000 | 9186 | Rat | 5.74 | 12.3 | 144 | 42.6 | 1061 | 1529 | (Gong et al., 2011) |
| Exenatide | PEG | 4186 | 20000 | 24186 | Rat | 5.74 | 37.4 | 144 | 4.58 | 1061 | 233 | (Gong et al., 2011) |
| Exenatide | PEG | 4186 | 30000 | 34186 | Rat | 5.74 | 76.4 | 144 | 2.61 | 1061 | 260 | (Gong et al., 2011) |
| Exenatide | PEG | 4186 | 40000 | 44186 | Rat | 5.74 | 69.8 | 144 | 2.37 | 1061 | 199 | (Gong et al., 2011) |
| Fab' | Albumin Binding | 50000 | 4000 | 54000 | Mouse | 1.63 | 25.3 | 152 | 4.17 | 230 | 112 | (Dennis et al., 2002) |
| Fab' | Albumin Binding | 50000 | 4000 | 54000 | Rabbit | 5.92 | 110 | 117 | 1.37 | 431 | 159 | (Dennis et al., 2002) |
| Fab' | Albumin Binding | 42000 | 5000 | 47000 | Mouse | 17.9 | 303 | 4.26 | 0.124 | 109 | 51.7 | (Zhang et al., 2021) |
| Fab' | Albumin Binding | 48000 | 5300 | 53300 | Mouse | 1.73 | 24.4 | 561 | 2.19 | 765 | 76.3 | (Schlapschy et al., 2013) |
| Fab' | PAS-100 | 48000 | 8500 | 56500 | Mouse | 1.73 | 2.07 | 561 | 74.8 | 765 | 129 | (Schlapschy et al., 2013) |
| Fab' | PAS-200 | 48000 | 18000 | 66000 | Mouse | 1.73 | 4.57 | 561 | 20.5 | 765 | 88.0 | (Schlapschy et al., 2013) |
| Fab' | PAS-200 | 48014 | 34298 | 82312 | Mouse | 9.52 | 64.7 | 4.83 | 0.942 | 28.0 | 71.7 | (Mazaheri et al., 2020) |
| Fab' | PAS-200 | 48000 | 34700 | 82700 | Mouse | 1.73 | 41.5 | 561 | 1.62 | 765 | 92.0 | (Schlapschy et al., 2013) |
| Fab' | PAS-400 | 48000 | 34500 | 82500 | Mouse | 1.73 | 14.9 | 561 | 5.88 | 765 | 104 | (Schlapschy et al., 2013) |
| Fab' | PAS-600 | 48000 | 51000 | 99000 | Mouse | 1.73 | 28.8 | 561 | 2.62 | 765 | 108 | (Schlapschy et al., 2013) |
| Fab' | PEG | 50000 | 5000 | 55000 | Rat | 13.8 | 53.6 | 30.8 | 7.90 | 505 | 326 | (Chapman et al., 1999) |
| Fab' | PEG | 50000 | 15000 | 65000 | Rat | 13.8 | 46.0 | 30.8 | 2.97 | 505 | 132 | (Chapman et al., 1999) |
| Fab' | PEG | 50000 | 20000 | 70000 | Rat | 1.49 | 42.6 | 186 | 3.62 | 306.8 | 150 | (Nakamura et al., 2020) |
| Fab' | PEG | 50000 | 25000 | 75000 | Rat | 26.1 | 32.7 | 18.8 | 2.88 | 646 | 96.9 | (Chapman et al., 1999) |
| Fab' | PEG | 50000 | 30000 | 80000 | Rat | 13.8 | 52.7 | 30.8 | 1.49 | 505 | 81.1 | (Chapman et al., 1999) |
| Fab' | PEG | 48000 | 40000 | 88000 | Mouse | 1.73 | 26.9 | 561 | 2.10 | 765 | 80.6 | (Schlapschy et al., 2013) |
| Fab' | PEG | 48014 | 40000 | 88014 | Mouse | 9.52 | 39.8 | 4.83 | 1.10 | 28.0 | 75.8 | (Mazaheri et al., 2020) |
| Fab' | PEG | 50000 | 40000 | 90000 | Rat | 26.1 | 46.4 | 18.8 | 1.70 | 646 | 105 | (Chapman et al., 1999) |
| Fab' | PEG | 45000 | 40000 | 85000 | Rat | 0.347 | 39.2 | 905 | 2.17 | 380 | 102 | (Selis et al., 2016) |
| Fab' | PEG | 50000 | 50000 | 100000 | Rat | 26.1 | 49.7 | 18.8 | 1.10 | 646 | 76.1 | (Chapman et al., 1999) |
| Fab' | Polysialic Acid | 50000 | 22000 | 72000 | Mouse | 0.155 | 0.175 | 3299 | 642 | 602 | 147 | (Constantinou et al., 2008) |
| Fab' | Polysialic Acid | 50000 | 99000 | 149000 | Mouse | 0.155 | 0.249 | 3299 | 663 | 602 | 192 | (Constantinou et al., 2008) |
| Fab' | Polysialic Acid | 50000 | 110000 | 160000 | Mouse | 0.155 | 0.253 | 3299 | 696 | 602 | 224 | (Constantinou et al., 2008) |
| Factor IX | Albumin, Human (Fusion) | 57000 | 65000 | 122000 | Human | 17.4 | 134 | 4.72 | 0.641 | 113 | 102 | (Santagostino et al., 2012) |
| Factor IX | Albumin, Human (Fusion) | 57000 | 65000 | 122000 | Mouse | 28.6 | 33.8 | 31.4 | 6.69 | 936 | 207 | (van der Flier et al., 2023) |
| Factor IX | Fc Fusion, Human IgG1 | 57000 | 50000 | 107000 | Human | 42.8 | 127 | 5.74 | 2.84 | 248 | 350 | (Powell et al., 2013) |
| Factor IX | Fc Fusion, Human IgG1 | 57000 | 50000 | 107000 | Mouse | 16.5 | 155 | 23.5 | 6.08 | 344 | 958 | (Peters et al., 2010) |
| Factor IX | Fc Fusion, Human IgG1 | 57000 | 50000 | 107000 | Mouse | 28.6 | 50.3 | 31.4 | 8.83 | 936 | 504 | (van der Flier et al., 2023) |
| Factor IX | PEG | 57000 | 40000 | 97000 | Human | 21.3 | 98.0 | 5.60 | 0.660 | 165 | 87.6 | (Negrier et al., 2011) |
| Factor VIIa | Albumin, Human (Fusion) | 52000 | 65000 | 117000 | Mouse | 0.550 | 3.33 | 243 | 17.5 | 196 | 83.1 | (Zollner et al., 2014) |
| Factor VIIa | Albumin, Human (Fusion) | 52000 | 65000 | 117000 | Rat | 0.831 | 4.94 | 139 | 10.1 | 153 | 59.8 | (Zollner et al., 2014) |
| Factor VIII | PEG | 275000 | 40000 | 315000 | Human | 11.6 | 13.8 | 2.78 | 1.59 | 37.9 | 31.1 | (Konkle et al., 2015) |
| Factor VIII | PEG (Branched) | 275000 | 20000 | 295000 | Human | 9.00 | 10.6 | 4.70 | 3.41 | 56.3 | 53.0 | (Mullins et al., 2017) |
| Factor VIII | Polysialic Acid | 275000 | 20000 | 295000 | Human | 17.0 | 21.2 | 2.71 | 1.76 | 43.3 | 47.0 | (Tiede et al., 2020) |
| Factor VIII | Polysialic Acid | 275000 | 20000 | 295000 | Monkey | 8.48 | 17.9 | 6.53 | 2.28 | 70.5 | 54.0 | (Glantschnig et al., 2019) |
| FB006 | Albumin Binding | 4330 | 340 | 4670 | Monkey | 6.53 | 117 | 59.0 | 1.92 | 182 | 257 | (Xie et al., 2010) |
| FB006 | Albumin Binding | 4330 | 340 | 4670 | Rat | 1.59 | 24.4 | 184 | 15.2 | 221 | 454 | (Xie et al., 2010) |
| FGF2 | PEG | 16293 | 20000 | 36293 | Rat | 1.28 | 2.19 | 557 | 167 | 833 | 511 | (Xie et al., 2010) |
| FGF21 | PEG | 19424 | 21912 | 41336 | Rat | 1.18 | 3.91 | 9411 | 1334 | 11536 | 7388 | (Huang et al., 2011) |
| G-CSF | Albumin, Human (Conjugate) | 18800 | 69200 | 88000 | Rat | 2.34 | 5.44 | 51.9 | 8.40 | 92.0 | 58.1 | (Paige et al., 1995) |
| G-CSF | Albumin, Human (Fusion) | 18800 | 65000 | 83800 | Mouse | 2.64 | 4.67 | 37.4 | 3.84 | 141 | 42.9 | (Halpern et al., 2002) |
| G-CSF | Albumin, Rat (Conjugate) | 18800 | 69200 | 88000 | Rat | 2.34 | 7.57 | 51.9 | 10.0 | 92.0 | 64.4 | (Paige et al., 1995) |
| G-CSF | Fc Fusion, Human IgG1 | 18987 | 53128 | 91102 | Rat | 1.38 | 4.18 | 49.9 | 2.65 | 89.4 | 28.4 | (Cox et al., 2004) |
| G-CSF | PEG | 18800 | 26200 | 45000 | Rat | 2.01 | 8.16 | 49.6 | 6.38 | 55.5 | 65.0 | (Tanaka et al., 1991) |
| GLP-1 | PEG | 3297 | 2000 | 5297 | Rat | 2.06 | 26.0 | 699 | 391 | 2406 | 8137 | (Lee et al., 2005) |
| GM-CSF | PEG | 14000 | 10000 | 24000 | Rat | 0.844 | 22.6 | 880 | 51.7 | 1385 | 656 | (Doherty et al., 2005) |
| GM-CSF | PEG | 14000 | 20000 | 34000 | Rat | 0.844 | 23.7 | 880 | 8.32 | 1385 | 117 | (Doherty et al., 2005) |
| GM-CSF | PEG | 14000 | 20000 | 34000 | Rat | 16.7 | 10.3 | 911 | 34.4 | 693 | 148 | (Cox et al., 2020) |
| GM-CSF | PEG | 14000 | 40000 | 54000 | Rat | 16.7 | 22.7 | 911 | 28.3 | 693 | 332 | (Cox et al., 2020) |
| Growth Hormone | Albumin, Human (Fusion) | 22162 | 65000 | 87162 | Rat | 3.19 | 1.97 | 35.5 | 32.9 | 54.6 | 70.0 | (Osborn et al., 2002) |
| Growth Hormone | PEG | 22000 | 20000 | 42000 | Rat | 1.85 | 12.5 | 52.9 | 9.71 | 14.3 | 34.3 | (Cox et al., 2007) |
| Growth Hormone | PEG | 22162 | 22000 | 44162 | Rat | 1.86 | 6.53 | 728 | 192 | 393 | 1222 | (da Silva Freitas et al., 2013) |
| Growth Hormone | PEG | 22162 | 22000 | 44162 | Rat | 1.86 | 4.48 | 728 | 110 | 393 | 474 | (da Silva Freitas et al., 2013) |
| Hirudin Mimetic | Albumin Binding | 2348 | 339 | 2687 | Rat | 0.442 | 3.01 | 2935 | 39.2 | 929 | 178 | (Liu et al., 2015) |
| Human Albumin | PEG | 66500 | 20000 | 86500 | Mouse | 17.5 | 29.4 | 15.0 | 5.04 | 305 | 172 | (Zhao et al., 2012a) |
| Human Albumin | PEG | 66500 | 20000 | 86500 | Mouse | 16.3 | 55.8 | 132 | 44.3 | 2975 | 2300 | (Zhao et al., 2012b) |
| i-body | Albumin Binding | 24747 | 2109 | 26856 | Mouse | 0.605 | 8.13 | 672 | 81.2 | 161 | 211 | (Griffiths et al., 2019) |
| i-body | PEG | 24747 | 30000 | 54747 | Mouse | 0.605 | 11.3 | 672 | 6.09 | 161 | 60.6 | (Griffiths et al., 2019) |
| i-body | PEG | 24747 | 40000 | 64747 | Mouse | 0.605 | 19.3 | 672 | 7.92 | 161 | 132 | (Griffiths et al., 2019) |
| IFN-alpha | Albumin Binding | 19300 | 15000 | 34300 | Rat | 1.21 | 25.7 | 311 | 2.72 | 271 | 86.1 | (Walker et al., 2010) |
| IFN-alpha | Albumin, Human (Fusion) | 19300 | 65000 | 84300 | Rat | 1.21 | 15.5 | 311 | 3.11 | 271 | 55.0 | (Walker et al., 2010) |
| IFN-alpha | Fc Fusion, Human IgG4 | 19300 | 50000 | 110000 | Rat | 13.6 | 32.4 | 25.0 | 2.14 | 421 | 77.0 | (Hsu et al., 2015) |
| IFN-α2 | PEG | 19000 | 10000 | 29000 | Rat | 0.438 | 21.9 | 2109 | 133 | 1286 | 1474 | (Rosendahl et al., 2005) |
| IFN-α2 | PEG | 19000 | 20000 | 39000 | Rat | 0.438 | 25.9 | 2109 | 47.6 | 1286 | 800 | (Rosendahl et al., 2005) |
| IFN-α2 | PEG | 19000 | 40000 | 59000 | Rat | 0.438 | 61.4 | 2109 | 10.2 | 1286 | 657 | (Rosendahl et al., 2005) |
| IFN-α2a | PEG (Trimer) | 19000 | 43000 | 62000 | Rat | 3.06 | 80.4 | 954 | 23.3 | 603 | 1912 | (Jo et al., 2006) |
| IFN-α2b | PAS-200 | 21000 | 16400 | 37400 | Mouse | 0.942 | 5.09 | 514 | 45.3 | 584 | 195 | (Schlapschy et al., 2013) |
| IFN--α2b | PAS-400 | 21000 | 33000 | 54000 | Mouse | 0.942 | 10.9 | 514 | 11.1 | 584 | 123 | (Schlapschy et al., 2013) |
| IFN--α2b | PAS-600 | 21000 | 49500 | 70500 | Mouse | 0.942 | 19.4 | 514 | 3.96 | 584 | 93.1 | (Schlapschy et al., 2013) |
| IFN-β1a | Albumin Binding | 23000 | 47000 | 70000 | Monkey | 6.15 | 50.8 | 61.8 | 2.97 | 403 | 169 | (Ji et al., 2019) |
| IFN-β1a | Albumin Binding | 23000 | 47000 | 70000 | Rat | 5.16 | 12.4 | 25.5 | 5.96 | 120 | 79.0 | (Ji et al., 2019) |
| IFN-β1a | PEG | 25000 | 20000 | 45000 | Rat | 1.10 | 13.0 | 56.7 | 4.98 | 68.7 | 39.2 | (Baker et al., 2006) |
| IFN-β1b | PEG (Branched) | 19300 | 40000 | 59300 | Rat | 1.93 | 18.4 | 229 | 4.42 | 427 | 89.4 | (Lee et al., 2013) |
| IgA | Albumin Binding | 160000 | 5000 | 165000 | Mouse | 33.3 | 42.3 | 4.80 | 0.873 | 145 | 47.6 | (Meyer et al., 2016) |
| IgA | Albumin Binding | 160000 | 5000 | 165000 | Mouse | 20.6 | 52.4 | 8.37 | 1.64 | 134 | 81.3 | (Meyer et al., 2016) |
| IgG | PEG | 150000 | 145000 | 295000 | Mouse | 167 | 77.9 | 0.582 | 0.629 | 142 | 74.5 | (Deckert et al., 2000) |
| IgG | PEG | 150000 | 187000 | 337000 | Mouse | 52.0 | 22.2 | 3.28 | 6.98 | 215 | 124 | (Wen et al., 2001) |
| IgG | PEG | 150000 | 300000 | 450000 | Mouse | 167 | 75.6 | 0.582 | 0.673 | 142 | 77.2 | (Deckert et al., 2000) |
| IL-10 | Fc Fusion, Human IgG1 | 35000 | 50000 | 120000 | Rat | 8.73 | 30.9 | 46.0 | 2.29 | 129 | 99.2 | (Guo et al., 2012) |
| IL-10 | PEG | 35000 | 7500 | 42500 | Mouse | 2.38 | 6.15 | 365 | 9.18 | 332 | 62.8 | (Alvarez et al., 2012) |
| IL-12 | Albumin Binding | 70000 | 30000 | 100000 | Mouse | 2.46 | 8.79 | 73.1 | 39.4 | 134 | 407 | (Cini et al., 2023) |
| IL-15 | Albumin Binding | 12900 | 30000 | 42900 | Mouse | 1.27 | 5.21 | 145 | 22.6 | 84.2 | 91.9 | (Cini et al., 2023) |
| IL-18BP | Albumin Binding | 20000 | 50000 | 70000 | Rat | 6.38 | 21.9 | 18.4 | 1.54 | 61.3 | 39.3 | (Jang et al., 2023) |
| IL-2 | Albumin Binding | 17216 | 1033 | 18249 | Mouse | 1.49 | 1.69 | 638 | 35.5 | 168 | 84.9 | (Qian et al., 2021) |
| IL-2 | Albumin Binding | 15500 | 5000 | 20500 | Mouse | 1.62 | 5.11 | 34520 | 4432 | 39482 | 31952 | (Adabi et al., 2017) |
| IL-2 | Albumin, Human (Fusion) | 15500 | 65000 | 80500 | Mouse | 0.301 | 6.10 | 304 | 6.71 | 86.1 | 52.1 | (Melder et al., 2005) |
| IL-2 | Albumin, Human (Fusion) | 15300 | 68700 | 84000 | Mouse | 0.408 | 7.19 | 1019 | 5.67 | 173 | 64.1 | (Merchant et al., 2022) |
| IL-24 | PEG | 23800 | 5000 | 28800 | Rat | 9.57 | 16.8 | 38164 | 10941 | 473034 | 168685 | (Zhang et al., 2019) |
| KGF-1 | PEG | 16298 | 20000 | 36998 | Rat | 2.46 | 23.3 | 14.2 | 7.12 | 48.7 | 123 | (Huang et al., 2012) |
| Lactoferrin | PEG (Branched) | 82679 | 42999 | 125678 | Rat | 0.122 | 0.229 | 766 | 43.2 | 156 | 24.8 | (Nojima et al., 2009) |
| Leuprolide | PEG | 1210 | 2000 | 3210 | Rat | 0.435 | 0.632 | 1469 | 659 | 818 | 390 | (Fu et al., 2020) |
| Leuprolide | PEG | 1210 | 5000 | 6210 | Rat | 0.435 | 3.44 | 1469 | 756 | 818 | 511 | (Fu et al., 2020) |
| LiTCo | Albumin, Human (Fusion) | 48000 | 62000 | 110000 | Mouse | 0.586 | 13.0 | 136 | 6.73 | 249 | 168 | (Hangiu et al., 2022) |
| LK8 | Fc Fusion, Human IgG1 | 12500 | 50000 | 75000 | Mouse | 0.596 | 42.3 | 1447 | 2.63 | 732 | 138 | (Yu et al., 2013) |
| Lysostaphin | Albumin Binding | 25000 | 5000 | 30000 | Rat | 2.09 | 7.88 | 303 | 3.98 | 938 | 38.7 | (Grishin et al., 2019) |
| Lysostaphin | PEG (Branched) | 27000 | 100000 | 127000 | Mouse | 4.28 | 14.9 | 22283 | 29.0 | 57610 | 532 | (Walsh et al., 2003) |
| MDTCS Fragment | Fc Fusion, Human IgG4 | 80000 | 60000 | 220000 | Mouse | 4.42 | 18.0 | 39.9 | 13.9 | 150 | 184 | (Kwak et al., 2024) |
| mmTRAIL | PEG | 60000 | 5000 | 65000 | Mouse | 1.79 | 4.43 | 2491 | 275 | 1040 | 929 | (Nie et al., 2017) |
| mmTRAIL | PEG | 60000 | 10000 | 70000 | Mouse | 1.79 | 11.1 | 2491 | 35.4 | 1040 | 321 | (Nie et al., 2017) |
| mmTRAIL | PEG | 60000 | 20000 | 80000 | Mouse | 1.79 | 13.1 | 2491 | 24.1 | 1040 | 312 | (Nie et al., 2017) |
| NELL-1 | PEG | 390000 | 473100 | 863100 | Mouse | 5.46 | 14.1 | 107 | 13.8 | 591 | 238 | (Kwak et al., 2015) |
| Oridonin | PEG | 364 | 10000 | 10364 | Rat | 1.73 | 16.4 | 688 | 242 | 1202 | 4283 | (Shen et al., 2013) |
| Oridonin | PEG | 364 | 20000 | 20364 | Rat | 1.73 | 43.9 | 688 | 151 | 1202 | 8411 | (Shen et al., 2013) |
| PAI-2 | PEG | 44891 | 20000 | 64891 | Mouse | 6.67 | 11.8 | 28.2 | 4.64 | 204 | 73.7 | (Vine et al., 2015) |
| Puerarin | PEG | 416 | 4700 | 5116 | Rat | 0.631 | 1.90 | 1978 | 3506 | 945 | 9242 | (Liu et al., 2010) |
| RGD | PEG | 1000 | 3400 | 4400 | Mouse | 1.77 | 18.1 | 10505 | 713 | 25265 | 18884 | (Chen et al., 2004) |
| Ribonuclease | PEG | 13600 | 44400 | 58000 | Rat | 1.92 | 107 | 244 | 1.02 | 293 | 149 | (Laznicek et al., 1993) |
| scFv | Albumin, Human (Fusion) | 26000 | 65000 | 91000 | Rat | 1.73 | 32.9 | 478 | 2.94 | 679 | 102 | (Evans et al., 2010) |
| scFv | Albumin, Human (Fusion) | 25000 | 67000 | 92000 | Mouse | 5.55 | 30.0 | 27.9 | 1.91 | 176 | 64.4 | (Berger et al., 2013) |
| scFv | PEG | 33000 | 20000 | 53000 | Mouse | 12.3 | 11.2 | 102 | 9.18 | 993 | 99.1 | (Kubetzko et al., 2006) |
| scFv | PEG | 25000 | 20000 | 45000 | Rat | 0.907 | 27.7 | 170 | 3.95 | 185 | 113 | (Reichard et al., 2016) |
| scFv | Polysialic Acid | 25000 | 12100 | 37100 | Mouse | 5.81 | 11.1 | 259 | 37.1 | 1300 | 387 | (Constantinou et al., 2009) |
| scFv | Polysialic Acid | 25000 | 15400 | 40400 | Mouse | 5.81 | 21.0 | 259 | 20.9 | 1300 | 535 | (Constantinou et al., 2009) |
| scFv | Polysialic Acid | 25000 | 16500 | 41500 | Mouse | 6.12 | 20.5 | 251 | 27.7 | 1262 | 659 | (Constantinou et al., 2009) |
| sdAb | Albumin Binding | 14700 | 6300 | 21000 | Mouse | 8.86 | 29.3 | 82.2 | 3.20 | 422 | 130 | (Xenaki et al., 2021) |
| sdAb | Albumin Binding | 13000 | 13000 | 26000 | Monkey | 7.09 | 14.7 | 93.0 | 1.03 | 251 | 43.2 | (Van Roy et al., 2015) |
| sdAb | Albumin Binding | 15000 | 15000 | 30000 | Mouse | 1.59 | 13.2 | 424 | 10.4 | 676 | 360 | (Glassman et al., 2020) |
| sdAb | PAS-200 | 15000 | 17000 | 32000 | Mouse | 0.823 | 6.36 | 50.2 | 17.5 | 52.3 | 85.5 | (Khodabakhsh et al., 2018) |
| sdAb | PEG | 11900 | 20000 | 31900 | Mouse | 1.32 | 6.18 | 388 | 19.3 | 737 | 142 | (Cong et al., 2012) |
| sdAb | PEG | 11900 | 40000 | 51900 | Mouse | 1.32 | 21.6 | 388 | 3.96 | 737 | 96.1 | (Cong et al., 2012) |
| Sonic Hedgehog | PEG | 20000 | 20000 | 40000 | Rat | 0.945 | 13.3 | 152 | 31.4 | 64.0 | 65.6 | (Pepinsky et al., 2002) |
| Sonic Hedgehog | PEG | 20000 | 40000 | 60000 | Rat | 0.945 | 12.7 | 152 | 2.50 | 64.0 | 36.6 | (Pepinsky et al., 2002) |
| Thymopentin | Albumin Binding | 680 | 338 | 1018 | Rat | 0.0707 | 2.07 | 10054 | 1171 | 934 | 2762 | (Tan et al., 2017) |
| TIMP2 | PEG | 14883 | 20000 | 34883 | Mouse | 5.16 | 27.9 | 41.3 | 3.51 | 197 | 134 | (Hayun et al., 2022) |
| TRAIL N109C | PEG | 66287 | 5000 | 71287 | Rat | 5.39 | 15.9 | 5.79 | 1.78 | 39.7 | 35.7 | (Pan et al., 2015) |
| Tricosanthin | PEG | 26000 | 5000 | 31000 | Rat | 0.785 | 3.60 | 766 | 191 | 179 | 581 | (He et al., 1999a) |
| Tricosanthin | PEG | 26000 | 5000 | 31000 | Rat | 0.642 | 2.01 | 805 | 245 | 209 | 394 | (An et al., 2007) |
| Tricosanthin | PEG | 26000 | 5000 | 31000 | Rat | 0.642 | 2.27 | 805 | 175 | 209 | 363 | (An et al., 2007) |
| Tricosanthin | PEG | 26000 | 20000 | 46000 | Rat | 0.785 | 3.41 | 766 | 16.4 | 179 | 79.0 | (He et al., 1999a) |
| Tricosanthin | PEG | 26000 | 33000 | 59000 | Rat | 0.764 | 2.19 | 581 | 184 | 106 | 520 | (He et al., 1999b) |
| Uricase | PAcM | 130000 | 270000 | 400000 | Mouse | 18.1 | 20.0 | 11.3 | 4.42 | 123 | 110 | (Caliceti et al., 1999) |
| Uricase | PEG | 130000 | 5000 | 135000 | Monkey | 1.76 | 158 | 15.1 | 0.221 | 20.8 | 46.5 | (Li et al., 2020) |
| Uricase | PEG | 135200 | 20000 | 155200 | Rat | 1.80 | 29.7 | 8.38 | 0.816 | 25.3 | 31.0 | (Nyborg et al., 2016) |
| Uricase | PEG | 135200 | 20000 | 155200 | Rat | 1.80 | 22.3 | 8.38 | 0.737 | 25.3 | 28.3 | (Nyborg et al., 2016) |
| Uricase | PEG | 130000 | 220000 | 350000 | Mouse | 18.1 | 30.3 | 11.3 | 1.89 | 123 | 77.4 | (Caliceti et al., 1999) |
| Uricase | PEG (Branched) | 130000 | 400000 | 530000 | Mouse | 18.1 | 31.2 | 11.3 | 1.72 | 123 | 71.3 | (Caliceti et al., 1999) |
| Uricase | PVP | 130000 | 250000 | 380000 | Mouse | 18.1 | 31.4 | 11.3 | 1.95 | 123 | 81.9 | (Caliceti et al., 1999) |

**Supplementary Table 1:** Complete dataset of half-life extension strategies used for analysis.

**References**

Adabi, E., Saebi, F., Moradi Hasan-Abad, A., Teimoori-Toolabi, L., Kardar, G.A., 2017. Evaluation of an Albumin-Binding Domain Protein Fused to Recombinant Human IL-2 and Its Effects on the Bioactivity and Serum Half-Life of the Cytokine. Iran Biomed J 21, 77-83.

Agerso, H., Stennicke, H.R., Pelzer, H., Olsen, E.N., Merricks, E.P., Defriess, N.A., Nichols, T.C., Ezban, M., 2012. Pharmacokinetics and pharmacodynamics of turoctocog alfa and N8-GP in haemophilia A dogs. Haemophilia 18, 941-947.

Aghaabdollahian, S., Ahangari Cohan, R., Norouzian, D., Davami, F., Asadi Karam, M.R., Torkashvand, F., Vaseghi, G., Moazzami, R., Latif Dizaji, S., 2019. Enhancing bioactivity, physicochemical, and pharmacokinetic properties of a nano-sized, anti-VEGFR2 Adnectin, through PASylation technology. Sci Rep 9, 2978.

Alvarez, H.M., So, O.Y., Hsieh, S., Shinsky-Bjorde, N., Ma, H., Song, Y., Pang, Y., Marian, M., Escandon, E., 2012. Effects of PEGylation and immune complex formation on the pharmacokinetics and biodistribution of recombinant interleukin 10 in mice. Drug Metab Dispos 40, 360-373.

An, Q., Lei, Y., Jia, N., Zhang, X., Bai, Y., Yi, J., Chen, R., Xia, A., Yang, J., Wei, S., Cheng, X., Fan, A., Mu, S., Xu, Z., 2007. Effect of site-directed PEGylation of trichosanthin on its biological activity, immunogenicity, and pharmacokinetics. Biomol Eng 24, 643-649.

Baker, D.P., Lin, E.Y., Lin, K., Pellegrini, M., Petter, R.C., Chen, L.L., Arduini, R.M., Brickelmaier, M., Wen, D., Hess, D.M., Chen, L., Grant, D., Whitty, A., Gill, A., Lindner, D.J., Pepinsky, R.B., 2006. N-terminally PEGylated human interferon-beta-1a with improved pharmacokinetic properties and in vivo efficacy in a melanoma angiogenesis model. Bioconjug Chem 17, 179-188.

Berger, V., Richter, F., Zettlitz, K., Unverdorben, F., Scheurich, P., Herrmann, A., Pfizenmaier, K., Kontermann, R.E., 2013. An anti-TNFR1 scFv-HSA fusion protein as selective antagonist of TNF action. Protein Eng Des Sel 26, 581-587.

Brandl, F., Merten, H., Zimmermann, M., Behe, M., Zangemeister-Wittke, U., Pluckthun, A., 2019. Influence of size and charge of unstructured polypeptides on pharmacokinetics and biodistribution of targeted fusion proteins. J Control Release 307, 379-392.

Caliceti, P., Schiavon, O., Veronese, F.M., 1999. Biopharmaceutical properties of uricase conjugated to neutral and amphiphilic polymers. Bioconjug Chem 10, 638-646.

Cao, N., Feng, S.S., 2008. Doxorubicin conjugated to D-alpha-tocopheryl polyethylene glycol 1000 succinate (TPGS): conjugation chemistry, characterization, in vitro and in vivo evaluation. Biomaterials 29, 3856-3865.

Chapman, A.P., Antoniw, P., Spitali, M., West, S., Stephens, S., King, D.J., 1999. Therapeutic antibody fragments with prolonged in vivo half-lives. Nat Biotechnol 17, 780-783.

Chen, X., Hou, Y., Tohme, M., Park, R., Khankaldyyan, V., Gonzales-Gomez, I., Bading, J.R., Laug, W.E., Conti, P.S., 2004. Pegylated Arg-Gly-Asp peptide: 64Cu labeling and PET imaging of brain tumor alphavbeta3-integrin expression. J Nucl Med 45, 1776-1783.

Cini, J.K., Dexter, S., Rezac, D.J., McAndrew, S.J., Hedou, G., Brody, R., Eraslan, R.N., Kenney, R.T., Mohan, P., 2023. SON-1210 - a novel bifunctional IL-12 / IL-15 fusion protein that improves cytokine half-life, targets tumors, and enhances therapeutic efficacy. Front Immunol 14, 1326927.

Cohan, R.A., Madadkar-Sobhani, A., Khanahmad, H., Roohvand, F., Aghasadeghi, M.R., Hedayati, M.H., Barghi, Z., Ardestani, M.S., Inanlou, D.N., Norouzian, D., 2011. Design, modeling, expression, and chemoselective PEGylation of a new nanosize cysteine analog of erythropoietin. Int J Nanomedicine 6, 1217-1227.

Cong, Y., Pawlisz, E., Bryant, P., Balan, S., Laurine, E., Tommasi, R., Singh, R., Dubey, S., Peciak, K., Bird, M., Sivasankar, A., Swierkosz, J., Muroni, M., Heidelberger, S., Farys, M., Khayrzad, F., Edwards, J., Badescu, G., Hodgson, I., Heise, C., Somavarapu, S., Liddell, J., Powell, K., Zloh, M., Choi, J.W., Godwin, A., Brocchini, S., 2012. Site-specific PEGylation at histidine tags. Bioconjug Chem 23, 248-263.

Constantinou, A., Epenetos, A.A., Hreczuk-Hirst, D., Jain, S., Deonarain, M.P., 2008. Modulation of antibody pharmacokinetics by chemical polysialylation. Bioconjug Chem 19, 643-650.

Constantinou, A., Epenetos, A.A., Hreczuk-Hirst, D., Jain, S., Wright, M., Chester, K.A., Deonarain, M.P., 2009. Site-specific polysialylation of an antitumor single-chain Fv fragment. Bioconjug Chem 20, 924-931.

Cox, G.N., Lee, J.I., Rosendahl, M.S., Chlipala, E.A., Doherty, D.H., 2020. Characterization of a Long-Acting Site-Specific PEGylated Murine GM-CSF Analog and Analysis of Its Hematopoietic Properties in Normal and Cyclophosphamide-Treated Neutropenic Rats. Protein J 39, 160-173.

Cox, G.N., Rosendahl, M.S., Chlipala, E.A., Smith, D.J., Carlson, S.J., Doherty, D.H., 2007. A long-acting, mono-PEGylated human growth hormone analog is a potent stimulator of weight gain and bone growth in hypophysectomized rats. Endocrinology 148, 1590-1597.

Cox, G.N., Smith, D.J., Carlson, S.J., Bendele, A.M., Chlipala, E.A., Doherty, D.H., 2004. Enhanced circulating half-life and hematopoietic properties of a human granulocyte colony-stimulating factor/immunoglobulin fusion protein. Exp Hematol 32, 441-449.

Coyle, T.E., Reding, M.T., Lin, J.C., Michaels, L.A., Shah, A., Powell, J., 2014. Phase I study of BAY 94-9027, a PEGylated B-domain-deleted recombinant factor VIII with an extended half-life, in subjects with hemophilia A. J Thromb Haemost 12, 488-496.

da Silva Freitas, D., Mero, A., Pasut, G., 2013. Chemical and enzymatic site specific PEGylation of hGH. Bioconjug Chem 24, 456-463.

Deckert, P.M., Jungbluth, A., Montalto, N., Clark, M.A., Finn, R.D., Williams, C., Jr., Richards, E.C., Panageas, K.S., Old, L.J., Welt, S., 2000. Pharmacokinetics and microdistribution of polyethylene glycol-modified humanized A33 antibody targeting colon cancer xenografts. Int J Cancer 87, 382-390.

Deng, N.H., Wang, L., He, Q.C., Zheng, J.C., Meng, Y., Meng, Y.F., Zhang, C.J., Shen, F.B., 2016. PEGylation alleviates the non-specific toxicities of Alpha-Momorcharin and preserves its antitumor efficacy in vivo. Drug Deliv 23, 95-100.

Dennis, M.S., Zhang, M., Meng, Y.G., Kadkhodayan, M., Kirchhofer, D., Combs, D., Damico, L.A., 2002. Albumin binding as a general strategy for improving the pharmacokinetics of proteins. J Biol Chem 277, 35035-35043.

Doherty, D.H., Rosendahl, M.S., Smith, D.J., Hughes, J.M., Chlipala, E.A., Cox, G.N., 2005. Site-specific PEGylation of engineered cysteine analogues of recombinant human granulocyte-macrophage colony-stimulating factor. Bioconjug Chem 16, 1291-1298.

Dumont, J.A., Liu, T., Low, S.C., Zhang, X., Kamphaus, G., Sakorafas, P., Fraley, C., Drager, D., Reidy, T., McCue, J., Franck, H.W., Merricks, E.P., Nichols, T.C., Bitonti, A.J., Pierce, G.F., Jiang, H., 2012. Prolonged activity of a recombinant factor VIII-Fc fusion protein in hemophilia A mice and dogs. Blood 119, 3024-3030.

Evans, L., Hughes, M., Waters, J., Cameron, J., Dodsworth, N., Tooth, D., Greenfield, A., Sleep, D., 2010. The production, characterisation and enhanced pharmacokinetics of scFv-albumin fusions expressed in Saccharomyces cerevisiae. Protein Expr Purif 73, 113-124.

Fu, M., Zhuang, X., Zhang, T., Guan, Y., Meng, Q., Zhang, Y., 2020. PEGylated leuprolide with improved pharmacokinetic properties. Bioorg Med Chem 28, 115306.

Glantschnig, H., Bauer, A., Benamara, K., Dockal, M., Ehrlich, V., Gritsch, H., Hobarth, G., Horling, F.M., Kopic, A., Leidenmuhler, P., Reipert, B.M., Rottensteiner, H., Ruthsatz, T., Schrenk, G., Schuster, M., Turecek, P.L., Weber, A., Wolfsegger, M., Scheiflinger, F., Hollriegl, W., 2019. Evaluation of Factor VIII Polysialylation: Identification of a Longer-Acting Experimental Therapy in Mice and Monkeys. J Pharmacol Exp Ther 371, 95-105.

Glassman, P.M., Walsh, L.R., Villa, C.H., Marcos-Contreras, O.A., Hood, E.D., Muzykantov, V.R., Greineder, C.F., 2020. Molecularly Engineered Nanobodies for Tunable Pharmacokinetics and Drug Delivery. Bioconjug Chem 31, 1144-1155.

Gong, N., Ma, A.N., Zhang, L.J., Luo, X.S., Zhang, Y.H., Xu, M., Wang, Y.X., 2011. Site-specific PEGylation of exenatide analogues markedly improved their glucoregulatory activity. Br J Pharmacol 163, 399-412.

Griffiths, K., Binder, U., McDowell, W., Tommasi, R., Frigerio, M., Darby, W.G., Hosking, C.G., Renaud, L., Machacek, M., Lloyd, P., Skerra, A., Foley, M., 2019. Half-life extension and non-human primate pharmacokinetic safety studies of i-body AD-114 targeting human CXCR4. MAbs 11, 1331-1340.

Grishin, A.V., Shestak, N.V., Lavrova, N.V., Lyashchuk, A.M., Popova, L.I., Strukova, N.V., Generalova, M.S., Ryazanova, A.V., Polyakov, N.B., Galushkina, Z.M., Soboleva, L.A., Boksha, I.S., Karyagina, A.S., Lunin, V.G., 2019. Fusion of Lysostaphin to an Albumin Binding Domain Prolongs Its Half-Life and Bactericidal Activity in the Systemic Circulation. Molecules 24.

Guo, L., Li, Z., Xu, B., Yu, M., Fu, Y., Liu, L., Wang, J., Luo, Y., 2019. Pharmacokinetics of PEGylated recombinant human endostatin in rhesus monkeys. Life Sci 238, 116967.

Guo, Y., Kang, W., Zhong, Y., Li, R., Li, G., Shen, Y., Hu, S., Sun, J., Xiao, W., 2012. Purification and characterization of human IL-10/Fc fusion protein expressed in Pichia pastoris. Protein Expr Purif 83, 152-156.

Halpern, W., Riccobene, T.A., Agostini, H., Baker, K., Stolow, D., Gu, M.L., Hirsch, J., Mahoney, A., Carrell, J., Boyd, E., Grzegorzewski, K.J., 2002. Albugranin, a recombinant human granulocyte colony stimulating factor (G-CSF) genetically fused to recombinant human albumin induces prolonged myelopoietic effects in mice and monkeys. Pharm Res 19, 1720-1729.

Hangiu, O., Compte, M., Dinesen, A., Navarro, R., Tapia-Galisteo, A., Mandrup, O.A., Erce-Llamazares, A., Lazaro-Gorines, R., Nehme-Alvarez, D., Dominguez-Alonso, C., Harwood, S.L., Alfonso, C., Blanco, B., Rubio-Perez, L., Jimenez-Reinoso, A., Diez-Alonso, L., Blanco, F.J., Sanz, L., Howard, K.A., Alvarez-Vallina, L., 2022. Tumor targeted 4-1BB agonist antibody-albumin fusions with high affinity to FcRn induce anti-tumor immunity without toxicity. iScience 25, 104958.

Hayun, H., Arkadash, V., Sananes, A., Arbely, E., Stepensky, D., Papo, N., 2022. Bioorthogonal PEGylation Prolongs the Elimination Half-Life of N-TIMP2 While Retaining MMP Inhibition. Bioconjug Chem 33, 795-806.

He, X.H., Shaw, P.C., Tam, S.C., 1999a. Reducing the immunogenicity and improving the in vivo activity of trichosanthin by site-directed pegylation. Life Sci 65, 355-368.

He, X.H., Shaw, P.C., Xu, L.H., Tam, S.C., 1999b. Site-directed polyethylene glycol modification of trichosanthin: effects on its biological activities, pharmacokinetics, and antigenicity. Life Sci 64, 1163-1175.

Hsu, W.C., Chien, Y.C., Chang, C.H., Yuan, T.T., Lee, T.W., Hwang, J.J., 2015. Characteristic Comparison Between 131I-Interferon-alpha and 131I-Interferon-alpha-Immunoglobulin-Fc Hybrid Protein in Rats Using Molecular Imaging. In Vivo 29, 445-452.

Huang, H., Fang, L., Xue, L., Zhang, T., Kim, K., Hou, S., Zheng, F., Zhan, C.G., 2019. PEGylation but Not Fc-Fusion Improves in Vivo Residence Time of a Thermostable Mutant of Bacterial Cocaine Esterase. Bioconjug Chem 30, 3021-3027.

Huang, Z., Wang, H., Lu, M., Sun, C., Wu, X., Tan, Y., Ye, C., Zhu, G., Wang, X., Cai, L., Li, X., 2011. A better anti-diabetic recombinant human fibroblast growth factor 21 (rhFGF21) modified with polyethylene glycol. PLoS One 6, e20669.

Huang, Z., Zhu, G., Sun, C., Zhang, J., Zhang, Y., Zhang, Y., Ye, C., Wang, X., Ilghari, D., Li, X., 2012. A novel solid-phase site-specific PEGylation enhances the in vitro and in vivo biostabilty of recombinant human keratinocyte growth factor 1. PLoS One 7, e36423.

Jang, Y.S., Lee, K., Park, M., Joo Park, J., Choi, G.M., Kim, C., Dehkohneh, S.B., Chi, S., Han, J., Song, M.Y., Han, Y.H., Cha, S.H., Goo Kang, S., 2023. Albumin-binding recombinant human IL-18BP ameliorates macrophage activation syndrome and atopic dermatitis via direct IL-18 inactivation. Cytokine 172, 156413.

Ji, S.I., Park, J.H., You, H.G., Chi, H.J., Bang, Y.W., Cha, S.H., 2019. Intact bioactivities and improved pharmacokinetic of the SL335-IFN-beta-1a fusion protein that created by genetic fusion of SL335, a human anti-serum albumin fab, and human interferon-beta. Immunol Lett 207, 46-55.

Jo, Y.W., Youn, Y.S., Lee, S.H., Kim, B.M., Kang, S.H., Yoo, M., Choi, E.C., Lee, K.C., 2006. Long-acting interferon-alpha 2a modified with a trimer-structured polyethylene glycol: preparation, in vitro bioactivity, in vivo stability and pharmacokinetics. Int J Pharm 309, 87-93.

Kenanova, V.E., Olafsen, T., Salazar, F.B., Williams, L.E., Knowles, S., Wu, A.M., 2010. Tuning the serum persistence of human serum albumin domain III:diabody fusion proteins. Protein Eng Des Sel 23, 789-798.

Khodabakhsh, F., Norouzian, D., Vaziri, B., Ahangari Cohan, R., Sardari, S., Mahboudi, F., Behdani, M., Mansouri, K., Mehdizadeh, A., 2018. Development of a novel nano-sized anti-VEGFA nanobody with enhanced physicochemical and pharmacokinetic properties. Artif Cells Nanomed Biotechnol 46, 1402-1414.

Kitamura, K., Takahashi, T., Takashina, K., Yamaguchi, T., Noguchi, A., Tsurumi, H., Toyokuni, T., Hakomori, S., 1990. Polyethylene glycol modification of the monoclonal antibody A7 enhances its tumor localization. Biochem Biophys Res Commun 171, 1387-1394.

Konkle, B.A., Stasyshyn, O., Chowdary, P., Bevan, D.H., Mant, T., Shima, M., Engl, W., Dyck-Jones, J., Fuerlinger, M., Patrone, L., Ewenstein, B., Abbuehl, B., 2015. Pegylated, full-length, recombinant factor VIII for prophylactic and on-demand treatment of severe hemophilia A. Blood 126, 1078-1085.

Koumenis, I.L., Shahrokh, Z., Leong, S., Hsei, V., Deforge, L., Zapata, G., 2000. Modulating pharmacokinetics of an anti-interleukin-8 F(ab')(2) by amine-specific PEGylation with preserved bioactivity. Int J Pharm 198, 83-95.

Kubetzko, S., Balic, E., Waibel, R., Zangemeister-Wittke, U., Pluckthun, A., 2006. PEGylation and multimerization of the anti-p185HER-2 single chain Fv fragment 4D5: effects on tumor targeting. J Biol Chem 281, 35186-35201.

Kubo, K., Tokashiki, M., Kuwasako, K., Tamura, M., Tsuda, S., Kubo, S., Yoshizawa-Kumagaye, K., Kato, J., Kitamura, K., 2014. Biological properties of adrenomedullin conjugated with polyethylene glycol. Peptides 57, 118-121.

Kunitomo, R., Miyauchi, Y., Inoue, M., 1992. Synthesis of a cytochrome c derivative with prolonged in vivo half-life and determination of ascorbyl radicals in the circulation of the rat. J Biol Chem 267, 8732-8738.

Kwak, H., Kim, M.S., Kim, S., Kim, J., Aoki, Y., Chung, S.J., Nam, H.J., Lee, W., 2024. Kinetic modeling of the plasma pharmacokinetic profiles of ADAMTS13 fragment and its Fc-fusion counterpart in mice. Front Pharmacol 15, 1352842.

Kwak, J.H., Zhang, Y., Park, J., Chen, E., Shen, J., Chawan, C., Tanjaya, J., Lee, S., Zhang, X., Wu, B.M., Ting, K., Soo, C., 2015. Pharmacokinetics and osteogenic potential of PEGylated NELL-1 in vivo after systemic administration. Biomaterials 57, 73-83.

Laznicek, M., Schiavon, O., Caliceti, P., Veronese, F.M., 1993. Pharmacokinetics and distribution of ribonuclease and its monomethoxypoly(ethylene glycol) derivatives in rats. Pharmacol Res 28, 153-161.

Lee, J.I., Eisenberg, S.P., Rosendahl, M.S., Chlipala, E.A., Brown, J.D., Doherty, D.H., Cox, G.N., 2013. Site-specific PEGylation enhances the pharmacokinetic properties and antitumor activity of interferon beta-1b. J Interferon Cytokine Res 33, 769-777.

Lee, S.H., Lee, S., Youn, Y.S., Na, D.H., Chae, S.Y., Byun, Y., Lee, K.C., 2005. Synthesis, characterization, and pharmacokinetic studies of PEGylated glucagon-like peptide-1. Bioconjug Chem 16, 377-382.

Li, H., Huo, J., Sun, D., Jiang, L., Hu, C., Bai, Y., Ma, X., Zhang, H., Shi, X., Zhao, Z., Zhou, J., Lu, Y., Zhang, C., 2020. Pharmacokinetics of Polyethylene Glycol-Modified Canine Uricase Following Single and Multiple Intravenous Injections in Cynomolgus Monkeys. Eur J Drug Metab Pharmacokinet 45, 445-451.

Li, L., Crow, D., Turatti, F., Bading, J.R., Anderson, A.L., Poku, E., Yazaki, P.J., Carmichael, J., Leong, D., Wheatcroft, D., Raubitschek, A.A., Hudson, P.J., Colcher, D., Shively, J.E., 2011. Site-specific conjugation of monodispersed DOTA-PEGn to a thiolated diabody reveals the effect of increasing peg size on kidney clearance and tumor uptake with improved 64-copper PET imaging. Bioconjug Chem 22, 709-716.

Li, Q., White, J.B., Peterson, N.C., Rickert, K.W., Lloyd, C.O., Allen, K.L., Rosenthal, K., Gao, X., Wu, H., Dall'Acqua, W.F., Borrok, M.J., Tsui, P., 2018. Tumor uptake of pegylated diabodies: Balancing systemic clearance and vascular transport. J Control Release 279, 126-135.

Lindhout, T., Iqbal, U., Willis, L.M., Reid, A.N., Li, J., Liu, X., Moreno, M., Wakarchuk, W.W., 2011. Site-specific enzymatic polysialylation of therapeutic proteins using bacterial enzymes. Proc Natl Acad Sci U S A 108, 7397-7402.

Liu, X., Zhi, H., Du, F., Ye, Z., Wang, N., Qin, W., Li, J., 2010. A HPLC-UV method for the determination of puerarin in rat plasma after intravenous administration of PEGylated puerarin conjugate. J Chromatogr B Analyt Technol Biomed Life Sci 878, 3297-3302.

Liu, Z., Yu, Z., Huang, Y., Zhang, Y., Han, G., Li, X., Dong, M., Yu, S., Wang, Y., Hu, J., Guo, H., Cheng, Y., Lv, L., Dai, Q., 2015. A novel stearic acid-modified hirudin peptidomimetic with improved pharmacokinetic properties and anticoagulant activity. Sci Rep 5, 14349.

Mazaheri, S., Talebkhan, Y., Mahboudi, F., Nematollahi, L., Cohan, R.A., Mirabzadeh Ardakani, E., Bayat, E., Sabzalinejad, M., Sardari, S., Torkashvand, F., 2020. Improvement of Certolizumab Fab' properties by PASylation technology. Sci Rep 10, 18464.

Melder, R.J., Osborn, B.L., Riccobene, T., Kanakaraj, P., Wei, P., Chen, G., Stolow, D., Halpern, W.G., Migone, T.S., Wang, Q., Grzegorzewski, K.J., Gallant, G., 2005. Pharmacokinetics and in vitro and in vivo anti-tumor response of an interleukin-2-human serum albumin fusion protein in mice. Cancer Immunol Immunother 54, 535-547.

Merchant, R., Galligan, C., Munegowda, M.A., Pearce, L.B., Lloyd, P., Smith, P., Merchant, F., To, M.D., 2022. Fine-tuned long-acting interleukin-2 superkine potentiates durable immune responses in mice and non-human primate. J Immunother Cancer 10.

Meyer, S., Nederend, M., Jansen, J.H., Reiding, K.R., Jacobino, S.R., Meeldijk, J., Bovenschen, N., Wuhrer, M., Valerius, T., Ubink, R., Boross, P., Rouwendal, G., Leusen, J.H., 2016. Improved in vivo anti-tumor effects of IgA-Her2 antibodies through half-life extension and serum exposure enhancement by FcRn targeting. MAbs 8, 87-98.

Mullins, E.S., Stasyshyn, O., Alvarez-Roman, M.T., Osman, D., Liesner, R., Engl, W., Sharkhawy, M., Abbuehl, B.E., 2017. Extended half-life pegylated, full-length recombinant factor VIII for prophylaxis in children with severe haemophilia A. Haemophilia 23, 238-246.

Nakamura, H., Anraku, M., Oda-Ueda, N., Ueda, T., Ohkuri, T., 2020. C-Terminal Cysteine PEGylation of Adalimumab Fab with an Engineered Interchain SS Bond. Biol Pharm Bull 43, 418-423.

Negrier, C., Knobe, K., Tiede, A., Giangrande, P., Moss, J., 2011. Enhanced pharmacokinetic properties of a glycoPEGylated recombinant factor IX: a first human dose trial in patients with hemophilia B. Blood 118, 2695-2701.

Nie, Q., Jia, D., Yang, H., Feng, Y., Fan, Q., Shi, Q., Wan, L., Lu, X., 2017. Conjugation to 10 kDa Linear PEG Extends Serum Half-Life and Preserves the Receptor-Binding Ability of mmTRAIL with Minimal Stimulation of PEG-Specific Antibodies. Mol Pharm 14, 502-512.

Nojima, Y., Suzuki, Y., Yoshida, K., Abe, F., Shiga, T., Takeuchi, T., Sugiyama, A., Shimizu, H., Sato, A., 2009. Lactoferrin conjugated with 40-kDa branched poly(ethylene glycol) has an improved circulating half-life. Pharm Res 26, 2125-2132.

Nyborg, A.C., Ward, C., Zacco, A., Chacko, B., Grinberg, L., Geoghegan, J.C., Bean, R., Wendeler, M., Bartnik, F., O'Connor, E., Gruia, F., Iyer, V., Feng, H., Roy, V., Berge, M., Miner, J.N., Wilson, D.M., Zhou, D., Nicholson, S., Wilker, C., Wu, C.Y., Wilson, S., Jermutus, L., Wu, H., Owen, D.A., Osbourn, J., Coats, S., Baca, M., 2016. A Therapeutic Uricase with Reduced Immunogenicity Risk and Improved Development Properties. PLoS One 11, e0167935.

Osborn, B.L., Sekut, L., Corcoran, M., Poortman, C., Sturm, B., Chen, G., Mather, D., Lin, H.L., Parry, T.J., 2002. Albutropin: a growth hormone-albumin fusion with improved pharmacokinetics and pharmacodynamics in rats and monkeys. Eur J Pharmacol 456, 149-158.

Paige, A.G., Whitcomb, K.L., Liu, J., Kinstler, O., 1995. Prolonged circulation of recombinant human granulocyte-colony stimulating factor by covalent linkage to albumin through a heterobifunctional polyethylene glycol. Pharm Res 12, 1883-1888.

Pan, L.Q., Zhao, W.B., Lai, J., Ding, D., Wei, X.Y., Li, Y.Y., Liu, W.H., Yang, X.Y., Xu, Y.C., Chen, S.Q., 2015. Hetero-modification of TRAIL trimer for improved drug delivery and in vivo antitumor activities. Sci Rep 5, 14872.

Pepinsky, R.B., Lee, W.C., Cornebise, M., Gill, A., Wortham, K., Chen, L.L., Leone, D.R., Giza, K., Dolinski, B.M., Perper, S., Nickerson-Nutter, C., Lepage, D., Chakraborty, A., Whalley, E.T., Petter, R.C., Adams, S.P., Lobb, R.R., Scott, D.M., 2005. Design, synthesis, and analysis of a polyethelene glycol-modified (PEGylated) small molecule inhibitor of integrin alpha4beta1 with improved pharmaceutical properties. J Pharmacol Exp Ther 312, 742-750.

Pepinsky, R.B., Shapiro, R.I., Wang, S., Chakraborty, A., Gill, A., Lepage, D.J., Wen, D., Rayhorn, P., Horan, G.S., Taylor, F.R., Garber, E.A., Galdes, A., Engber, T.M., 2002. Long-acting forms of Sonic hedgehog with improved pharmacokinetic and pharmacodynamic properties are efficacious in a nerve injury model. J Pharm Sci 91, 371-387.

Peters, R.T., Low, S.C., Kamphaus, G.D., Dumont, J.A., Amari, J.V., Lu, Q., Zarbis-Papastoitsis, G., Reidy, T.J., Merricks, E.P., Nichols, T.C., Bitonti, A.J., 2010. Prolonged activity of factor IX as a monomeric Fc fusion protein. Blood 115, 2057-2064.

Pink, A., Kallastu, A., Turkina, M., Skolnaja, M., Kogerman, P., Pall, T., Valkna, A., 2014. Purification, characterization and plasma half-life of PEGylated soluble recombinant non-HA-binding CD44. BioDrugs 28, 393-402.

Powell, J.S., Josephson, N.C., Quon, D., Ragni, M.V., Cheng, G., Li, E., Jiang, H., Li, L., Dumont, J.A., Goyal, J., Zhang, X., Sommer, J., McCue, J., Barbetti, M., Luk, A., Pierce, G.F., 2012. Safety and prolonged activity of recombinant factor VIII Fc fusion protein in hemophilia A patients. Blood 119, 3031-3037.

Powell, J.S., Pasi, K.J., Ragni, M.V., Ozelo, M.C., Valentino, L.A., Mahlangu, J.N., Josephson, N.C., Perry, D., Manco-Johnson, M.J., Apte, S., Baker, R.I., Chan, G.C., Novitzky, N., Wong, R.S., Krassova, S., Allen, G., Jiang, H., Innes, A., Li, S., Cristiano, L.M., Goyal, J., Sommer, J.M., Dumont, J.A., Nugent, K., Vigliani, G., Brennan, A., Luk, A., Pierce, G.F., Investigators, B.L., 2013. Phase 3 study of recombinant factor IX Fc fusion protein in hemophilia B. N Engl J Med 369, 2313-2323.

Qian, M., Zhang, Q., Lu, J., Zhang, J., Wang, Y., Shangguan, W., Feng, M., Feng, J., 2021. Long-Acting Human Interleukin 2 Bioconjugate Modified with Fatty Acids by Sortase A. Bioconjug Chem 32, 615-625.

Reichard, E.E., Nanaware-Kharade, N., Gonzalez, G.A., 3rd, Thakkar, S., Owens, S.M., Peterson, E.C., 2016. PEGylation of a High-Affinity Anti-(+)Methamphetamine Single Chain Antibody Fragment Extends Functional Half-Life by Reducing Clearance. Pharm Res 33, 2954-2966.

Rosendahl, M.S., Doherty, D.H., Smith, D.J., Carlson, S.J., Chlipala, E.A., Cox, G.N., 2005. A long-acting, highly potent interferon alpha-2 conjugate created using site-specific PEGylation. Bioconjug Chem 16, 200-207.

Santagostino, E., Negrier, C., Klamroth, R., Tiede, A., Pabinger-Fasching, I., Voigt, C., Jacobs, I., Morfini, M., 2012. Safety and pharmacokinetics of a novel recombinant fusion protein linking coagulation factor IX with albumin (rIX-FP) in hemophilia B patients. Blood 120, 2405-2411.

Schlapschy, M., Binder, U., Borger, C., Theobald, I., Wachinger, K., Kisling, S., Haller, D., Skerra, A., 2013. PASylation: a biological alternative to PEGylation for extending the plasma half-life of pharmaceutically active proteins. Protein Eng Des Sel 26, 489-501.

Selis, F., Foca, G., Sandomenico, A., Marra, C., Di Mauro, C., Saccani Jotti, G., Scaramuzza, S., Politano, A., Sanna, R., Ruvo, M., Tonon, G., 2016. Pegylated Trastuzumab Fragments Acquire an Increased in Vivo Stability but Show a Largely Reduced Affinity for the Target Antigen. Int J Mol Sci 17, 491.

Shen, J., Zhang, D., Zhao, Z., Jia, L., Zheng, D., Liu, G., Hao, L., Zhang, Q., Tian, X., Li, C., Guo, H., 2013. Synthesis, characterization, in vitro and in vivo evaluation of PEGylated oridonin conjugates. Int J Pharm 456, 80-86.

Simon, M., Stefan, N., Borsig, L., Pluckthun, A., Zangemeister-Wittke, U., 2014. Increasing the antitumor effect of an EpCAM-targeting fusion toxin by facile click PEGylation. Mol Cancer Ther 13, 375-385.

Tan, Y., Wang, W., Wu, C., Pan, Z., Yao, G., Fang, L., Su, W., 2017. Myristic acid-modified thymopentin for enhanced plasma stability and immune-modulating activity. Int Immunopharmacol 47, 88-94.

Tanaka, H., Satake-Ishikawa, R., Ishikawa, M., Matsuki, S., Asano, K., 1991. Pharmacokinetics of recombinant human granulocyte colony-stimulating factor conjugated to polyethylene glycol in rats. Cancer Res 51, 3710-3714.

Tiede, A., Allen, G., Bauer, A., Chowdary, P., Collins, P., Goldstein, B., Jiang, H.J., Kӧck, K., Takacs, I., Timofeeva, M., Wolfsegger, M., Srivastava, S., 2020. SHP656, a polysialylated recombinant factor VIII (PSA-rFVIII): First-in-human study evaluating safety, tolerability and pharmacokinetics in patients with severe haemophilia A. Haemophilia 26, 47-55.

Ton, G.N., Weichert, J.P., Longino, M.A., Fine, J.P., Kwon, G.S., 2005. Methoxypoly(ethylene glycol)-conjugated carboxypeptidase A for solid tumor targeting: part II: pharmacokinetics and biodistribution in normal and tumor-bearing rodents. J Control Release 104, 155-166.

van der Flier, A., Hong, V., Liu, Z., Piepenhagen, P., Ulinski, G., Dumont, J.A., Orcutt, K.D., Goel, A., Peters, R., Salas, J., 2023. Biodistribution of recombinant factor IX, extended half-life recombinant factor IX Fc fusion protein, and glycoPEGylated recombinant factor IX in hemophilia B mice. Blood Coagul Fibrinolysis 34, 353-363.

Van Roy, M., Ververken, C., Beirnaert, E., Hoefman, S., Kolkman, J., Vierboom, M., Breedveld, E., t Hart, B., Poelmans, S., Bontinck, L., Hemeryck, A., Jacobs, S., Baumeister, J., Ulrichts, H., 2015. The preclinical pharmacology of the high affinity anti-IL-6R Nanobody(R) ALX-0061 supports its clinical development in rheumatoid arthritis. Arthritis Res Ther 17, 135.

Vine, K.L., Lobov, S., Indira Chandran, V., Harris, N.L., Ranson, M., 2015. Improved pharmacokinetic and biodistribution properties of the selective urokinase inhibitor PAI-2 (SerpinB2) by site-specific PEGylation: implications for drug delivery. Pharm Res 32, 1045-1054.

Walker, A., Dunlevy, G., Rycroft, D., Topley, P., Holt, L.J., Herbert, T., Davies, M., Cook, F., Holmes, S., Jespers, L., Herring, C., 2010. Anti-serum albumin domain antibodies in the development of highly potent, efficacious and long-acting interferon. Protein Eng Des Sel 23, 271-278.

Walsh, S., Shah, A., Mond, J., 2003. Improved pharmacokinetics and reduced antibody reactivity of lysostaphin conjugated to polyethylene glycol. Antimicrob Agents Chemother 47, 554-558.

Wen, X., Wu, Q.P., Lu, Y., Fan, Z., Charnsangavej, C., Wallace, S., Chow, D., Li, C., 2001. Poly(ethylene glycol)-conjugated anti-EGF receptor antibody C225 with radiometal chelator attached to the termini of polymer chains. Bioconjug Chem 12, 545-553.

Xenaki, K.T., Dorrestijn, B., Muns, J.A., Adamzek, K., Doulkeridou, S., Houthoff, H., Oliveira, S., van Bergen En Henegouwen, P.M., 2021. Homogeneous tumor targeting with a single dose of HER2-targeted albumin-binding domain-fused nanobody-drug conjugates results in long-lasting tumor remission in mice. Theranostics 11, 5525-5538.

Xie, D., Yao, C., Wang, L., Min, W., Xu, J., Xiao, J., Huang, M., Chen, B., Liu, B., Li, X., Jiang, H., 2010. An albumin-conjugated peptide exhibits potent anti-HIV activity and long in vivo half-life. Antimicrob Agents Chemother 54, 191-196.

Xu, L., Zhang, C., Liu, L., Zhang, Y., Wang, Q., Wang, J., Liu, Y., Su, Z., 2017. Purification and characterization of a long-acting ciliary neurotrophic factor via genetically fused with an albumin-binding domain. Protein Expr Purif 139, 14-20.

Yu, H.K., Lee, H.J., Ahn, J.H., Lim, I.H., Moon, J.H., Yoon, Y., Yi, L.S., Kim, S.J., Kim, J.S., 2013. Immunoglobulin Fc domain fusion to apolipoprotein(a) kringle V significantly prolongs plasma half-life without affecting its anti-angiogenic activity. Protein Eng Des Sel 26, 425-432.

Zhang, Q., Qian, M., Wu, Y., Wang, Y., Shangguan, W., Lu, J., Zhao, W., Feng, J., 2021. Design and biological evaluation of novel long-acting adalimumab Fab conjugated with the albumin binding domain. Eur J Pharmacol 904, 174152.

Zhang, Y., Ma, Q., Wang, J., Ge, J., Hua, J., Shi, Y., Zhang, C., Liu, M., Wang, Y., Chen, Z., Wang, Z., Liu, Y., Jiang, H., 2019. Expression, Purification, and Polyethylene Glycol Site-Specific Modification of Recombinant Human Interleukin 24 in Escherichia coli. Protein J 38, 576-585.

Zhao, T., Cheng, Y.N., Tan, H.N., Liu, J.F., Xu, H.L., Pang, G.L., Wang, F.S., 2012a. Site-specific chemical modification of human serum albumin with polyethylene glycol prolongs half-life and improves intravascular retention in mice. Biol Pharm Bull 35, 280-288.

Zhao, T., Yang, Y., Zong, A., Tan, H., Song, X., Meng, S., Song, C., Pang, G., Wang, F., 2012b. N-terminal PEGylation of human serum albumin and investigation of its pharmacokinetics and pulmonary microvascular retention. Biosci Trends 6, 81-88.

Zheng, F., Jin, Z., Deng, J., Chen, X., Zheng, X., Wang, G., Kim, K., Shang, L., Zhou, Z., Zhan, C.G., 2022. Development of a Highly Efficient Long-Acting Cocaine Hydrolase Entity to Accelerate Cocaine Metabolism. Bioconjug Chem 33, 1340-1349.

Zollner, S., Schuermann, D., Raquet, E., Mueller-Cohrs, J., Weimer, T., Pragst, I., Dickneite, G., Schulte, S., 2014. Pharmacological characteristics of a novel, recombinant fusion protein linking coagulation factor VIIa with albumin (rVIIa-FP). J Thromb Haemost 12, 220-228.