**Supporting Information for**

Different intermolecular interactions drive nonpathogenic liquid-liquid phase separation and potentially pathogenic fibril formation by TDP-43

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**Other supporting materials for this manuscript include the following:**

Movies S1 to S10



Fig. S1

**The comparison of TDP-43 LCD at different condition. (a)** Turbidity (OD600 values) of TDP-43 LCD solutions in four different conditions. (blank, pH 6.0 10 mM phosphate buffer; PB, 100 μM protein concentration in pH 6.0 10 mM phosphate buffer; PB+RNA, 100 μM protein concentration in pH 6.0 10 mM phosphate buffer with yeast RNA (20ng/μL); PB+Urea, 100 μM protein concentration in the same PB buffer and 150mM urea). Error bars represent SD of three replicates. **(b)** Liquid-like droplets were imaged by negative-staining TEM, while enlarged images were presented below. (PB, pH 6.0 10mM phosphate buffer; PB+RNA, pH 6.0 10mM phosphate buffer with yeast RNA (20ng/μL). Both samples were at a concentration of 100 μM. **(c)** Force profile of the right droplet shown in figure 1a bottom panel during the forced fusion process was recorded in VideoS2 using the optical tweezer. Red arrows represented the many attempts forcing the droplets closer together.



Fig. S2

**The concentration effect on TDP-43 LCD in PB buffer (a)** Image of TDP-43 LCD LLPS in 200 μM protein concentration in pH 6.0 10 mM phosphate buffer (PB) by DIC microscopy; **(b)** Image of TDP-43 LCD LLPS in 200 μM protein concentration in pH 6.0 10 mM phosphate buffer (PB) by DIC microscopy; **(c)** Turbidity (OD600 values) of TDP-43 LCD solutions in three different protein concentrations in the same PB buffer. Error bars represent SD of three replicates.

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**Fig. S3**

**TDP-43 LCD ThT fluorescence changes in different conditions and its 1H-15N HSQC spectra comparison (a)** ThT fluorescence changes of 100 μM TDP-43 LCD in different conditions. All solutions were in pH 6.0 10 mM phosphate buffer, with PB+RNA containing yeast RNA (20ng/μL) and PB+urea containing 150 mM urea. Error bars represent SD of three replicates. **(b)** 15N chemical shift differences (Δδ15N) obtained from the 1H-15N HSQC spectra. Δδ15N= δ15N (MES, pH5.5)- δ15N (MES, pH6.1). **(c)** The NMR signal intensities from 1H-15N HSQC spectra of TDP-43 LCD (100 μm) in pH6.0 10mM phosphate buffer (in red) and TDP-43 LCD (70 μm) in pH5.5 20mM MES buffer (in green) obtained within 2 hours from the sample preparation. **(d)** 15N chemical shift differences (Δδ15N) obtained from the 1H-15N HSQC spectra. Δδ15N= δ15N (PB)- δ15N (MES, pH5.5). **(e)** The NMR signal intensity changes with time. Red color indicates the residue signal intensity from 1H-15N HSQC spectrum of TDP-43 LCD (100 μM) in pH6.0 10mM phosphate buffer with 150mM urea, obtained within 2 hours from sample preparation (labeled as I1h using the average time) and blue color indicates the spectrum obtained at ~22h from the sample preparation.

Table S1. Amino acid Composition of TDP-43 LCD (a) the full sequence, (b) TDP-43 LCD without the helical segment (residue 320-343), (c) TDP-43 LCD helical segment (residue 320-343)

|  |  |  |
| --- | --- | --- |
| **a. Amino acid Composition of TDP-43 LCD** | | |
| **Number of Amino acid Residues** | **Amino acid Type** | **Fractional population** |
| 38 | Gly | 25.7 |
| 23 | Ser | 15.5 |
| 20 | Asn | 13.5 |
| 14 | Ala | 9.5 |
| 12 | Gln | 8.1 |
| 10 | Met | 6.8 |
| 8 | Phe | 5.4 |
| 5 | Arg | 3.4 |
| 4 | Leu | 2.7 |
| 4 | Pro | 2.7 |
| 3 | Trp | 2 |
| 2 | Glu | 1.4 |
| 2 | Ile | 1.4 |
| 1 | Asp | 0.7 |
| 1 | Lys | 0.7 |
| 1 | Tyr | 0.7 |
| 0 | Cys | 0 |
| 0 | His | 0 |
| 0 | Thr | 0 |
| 0 | Val | 0 |

|  |  |  |
| --- | --- | --- |
| **b. Amino acid Composition of TDP-43 LCD without helical segment** | | |
| **Number of Amino acid Residues** | **Amino acid Type** | **Fractional population** |
| 36 | Gly | 28.8 |
| 20 | Asn | 16 |
| 20 | Ser | 16 |
| 9 | Gln | 7.2 |
| 8 | Phe | 6.4 |
| 7 | Ala | 5.6 |
| 5 | Arg | 4 |
| 5 | Met | 4 |
| 4 | Pro | 3.2 |
| 2 | Glu | 1.6 |
| 2 | Ile | 1.6 |
| 2 | Leu | 1.6 |
| 2 | Trp | 1.6 |
| 1 | Asp | 0.8 |
| 1 | Lys | 0.8 |
| 1 | Tyr | 0.8 |
| 0 | Cys | 0 |
| 0 | His | 0 |
| 0 | Thr | 0 |
| 0 | Val | 0 |

|  |  |  |
| --- | --- | --- |
| **c. Amino acid Composition of TDP-43 LCD helical segment** | | |
| **Number of Amino acid Residues** | **Amino acid Type** | **Fractional population** |
| 7 | Ala | 30.4 |
| 5 | Met | 21.7 |
| 3 | Gln | 13 |
| 3 | Ser | 13 |
| 2 | Gly | 8.7 |
| 2 | Leu | 8.7 |
| 1 | Trp | 4.3 |
| 0 | Arg | 0 |
| 0 | Asn | 0 |
| 0 | Asp | 0 |
| 0 | Cys | 0 |
| 0 | Glu | 0 |
| 0 | His | 0 |
| 0 | Ile | 0 |
| 0 | Lys | 0 |
| 0 | Phe | 0 |
| 0 | Pro | 0 |
| 0 | Thr | 0 |
| 0 | Tyr | 0 |
| 0 | Val | 0 |

Table S2. 1H, 15N chemical shifts from four published work (BMRB 26823, 50154, 26728, 26816).

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| BMRB: 26823 | | | BMRB: 50154 | | | BMRB: 26728 | | | BMRB: 26816 | | |
| 20 M, pH 6.1 20 mM MES, 298K | | | 110 M, pH4.0, 1 mM CD3COOD, 298K | | | 100 M, pH 6.5, 10 mM PB, 283K | | | 0.8 mM, pH 2.5, 8 M Urea, 283K | | |
|  | 15N | 1H |  | 15N | 1H |  | 15N | 1H |  | 15N | 1H |
| - | - | - | 266 | 121.443 | 8.41 | 266 | 118.133 | 8.619 | 266 | 118.135 | 8.661 |
| - | - | - | 267 | 120.537 | 8.482 | 267 | 120.961 | 8.578 | 267 | 121.438 | 8.646 |
| - | - | - | 268 | 121.938 | 8.355 | 268 | 121.73 | 8.418 | 268 | 122.091 | 8.488 |
| 269 | 121.088 | 8.405 | 269 | 120.91 | 8.369 | 269 | 121.193 | 8.496 | 269 | 122.099 | 8.583 |
| 270 | 122.907 | 8.2 | 270 | 122.796 | 8.147 | 270 | 123.109 | 8.321 | 270 | 124.229 | 8.446 |
| 271 | 121.834 | 8.326 | 271 | 121.108 | 8.24 | 271 | 121.914 | 8.455 | 271 | 122.005 | 8.566 |
| 272 | 121.842 | 8.367 | 272 | 121.961 | 8.334 | 272 | 122.152 | 8.493 | 272 | 123.316 | 8.64 |
| 273 | 116.31 | 8.278 | 273 | 116.406 | 8.273 | 273 | 116.674 | 8.441 | 273 | 117.443 | 8.57 |
| 274 | 110.444 | 8.379 | 274 | 110.64 | 8.367 | 274 | 110.746 | 8.517 | 274 | 110.828 | 8.546 |
| 275 | 120.341 | 8.067 | 275 | 120.357 | 8.071 | 275 | 120.582 | 8.202 | 275 | 120.858 | 8.299 |
| 276 | 120.864 | 8.315 | 276 | 120.915 | 8.298 | 276 | 121.154 | 8.481 | 276 | 121.697 | 8.545 |
| 277 | 110.717 | 8.269 | 277 | 110.658 | 8.245 | 277 | 111.027 | 8.403 | 277 | 111.178 | 8.437 |
| 278 | 107.819 | 7.894 | 278 | 107.88 | 7.891 | 278 | 107.975 | 8.005 | 278 | 108.016 | 7.981 |
| 279 | 119.017 | 8.336 | 279 | 119.052 | 8.324 | 279 | 119.17 | 8.492 | 279 | 119.294 | 8.583 |
| 281 | 108.617 | 8.385 | 281 | 108.664 | 8.357 | 281 | 108.961 | 8.537 | 281 | 108.78 | 8.491 |
| 282 | 108.134 | 8.036 | 282 | 108.177 | 8.029 | 282 | 108.33 | 8.156 | 282 | 108.368 | 8.17 |
| 283 | 119.7 | 8.138 | 283 | 119.704 | 8.117 | 283 | 119.944 | 8.277 | 283 | 119.89 | 8.309 |
| 284 | 110.247 | 8.393 | 284 | 110.579 | 8.381 | 284 | 110.544 | 8.536 | 284 | 110.482 | 8.529 |
| 285 | 118.629 | 8.27 | 285 | 118.605 | 8.259 | 285 | 118.788 | 8.408 | 285 | 118.985 | 8.459 |
| 286 | 120.46 | 8.452 | 286 | 120.495 | 8.438 | 286 | 120.688 | 8.599 | 286 | 120.929 | 8.629 |
| 287 | 109.388 | 8.379 | 287 | 109.406 | 8.358 | 287 | 109.701 | 8.515 | 287 | 109.646 | 8.489 |
| 288 | 108.103 | 8.031 | 288 | 108.332 | 8.098 | 288 | 108.457 | 8.234 | 288 | 108.482 | 8.245 |
| 289 | 119.685 | 8.141 | 289 | 119.748 | 8.123 | 289 | 119.852 | 8.288 | 289 | 119.854 | 8.313 |
| 290 | 110.247 | 8.395 | 290 | 110.259 | 8.383 | 290 | 110.546 | 8.538 | 290 | 110.517 | 8.53 |
| 291 | 118.573 | 8.273 | 291 | 118.741 | 8.257 | 291 | 118.898 | 8.402 | 291 | 119.008 | 8.436 |
| 292 | 116.153 | 8.31 | 292 | 116.216 | 8.302 | 292 | 116.456 | 8.459 | 292 | 116.746 | 8.519 |
| 293 | 122.429 | 8.369 | 293 | 122.491 | 8.361 | 293 | 122.749 | 8.522 | 293 | 123.019 | 8.571 |
| 294 | 109.46 | 8.322 | 294 | 109.491 | 8.308 | 294 | 109.762 | 8.5 | 294 | 109.756 | 8.461 |
| 295 | 108.594 | 8.26 | 295 | 108.652 | 8.244 | 295 | 108.793 | 8.39 | 295 | 108.706 | 8.375 |
| 296 | 108.51 | 8.273 | 296 | 108.792 | 8.277 | 296 | 108.974 | 8.424 | 296 | 108.915 | 8.414 |
| 297 | 123.624 | 8.232 | 297 | 123.639 | 8.214 | 297 | 123.756 | 8.376 | 297 | 123.75 | 8.382 |
| 298 | 107.952 | 8.355 | 298 | 107.967 | 8.341 | 298 | 108.172 | 8.491 | 298 | 108.22 | 8.484 |
| 299 | 121.267 | 8.096 | 299 | 121.279 | 8.077 | 299 | 121.385 | 8.24 | 299 | 121.46 | 8.248 |
| 300 | 109.107 | 8.413 | 300 | 109.133 | 8.388 | 300 | 109.368 | 8.551 | 300 | 109.413 | 8.543 |
| 301 | 118.553 | 8.272 | 301 | 118.472 | 8.268 | 301 | 118.627 | 8.416 | 301 | 118.764 | 8.458 |
| 302 | 119.004 | 8.459 | 302 | 119.102 | 8.463 | 302 | 119.245 | 8.599 | 302 | 119.632 | 8.655 |
| 303 | 120.366 | 8.336 | 303 | 120.239 | 8.351 | 303 | 120.585 | 8.469 | 303 | 120.877 | 8.497 |
| 304 | 109.47 | 8.387 | 304 | 109.473 | 8.37 | 304 | 109.526 | 8.506 | 304 | 109.785 | 8.487 |
| 305 | 115.406 | 8.176 | 305 | 115.404 | 8.167 | 305 | 115.579 | 8.314 | 305 | 115.509 | 8.339 |
| 306 | 120.415 | 8.493 | 306 | 120.581 | 8.481 | 306 | 120.673 | 8.634 | 306 | 121.11 | 8.704 |
| 307 | 120.289 | 8.303 | 307 | 120.314 | 8.3 | 307 | 120.508 | 8.439 | 307 | 120.859 | 8.489 |
| 308 | 109.539 | 8.372 | 308 | 109.455 | 8.362 | 308 | 109.697 | 8.461 | 308 | 109.782 | 8.49 |
| 309 | 108.577 | 8.233 | 309 | 108.601 | 8.219 | 309 | 108.758 | 8.361 | 309 | 108.662 | 8.355 |
| 310 | 108.753 | 8.29 | 310 | 108.596 | 8.262 | 310 | 108.727 | 8.407 | 310 | 108.759 | 8.407 |
| 311 | 119.353 | 8.173 | 311 | 119.426 | 8.167 | 311 | 119.529 | 8.315 | 311 | 119.722 | 8.384 |
| 312 | 119.372 | 8.314 | 312 | 119.416 | 8.313 | 312 | 119.621 | 8.459 | 312 | 120.085 | 8.566 |
| 313 | 120.878 | 8.214 | 313 | 120.861 | 8.19 | 313 | 121.166 | 8.357 | 313 | 121.454 | 8.416 |
| 314 | 109.861 | 8.281 | 314 | 109.971 | 8.271 | 314 | 110.17 | 8.413 | 314 | 110.15 | 8.44 |
| 315 | 123.571 | 7.994 | 315 | 123.544 | 7.972 | 315 | 123.73 | 8.131 | 315 | 123.728 | 8.148 |
| 316 | 118.141 | 8.025 | 316 | 118.211 | 8.028 | 316 | 118.498 | 8.188 | 316 | 119.025 | 8.269 |
| 317 | 116.568 | 8.013 | 317 | 116.736 | 8.023 | 317 | 117.027 | 8.145 | 317 | 117.694 | 8.311 |
| 318 | 121.334 | 7.985 | 318 | 121.498 | 7.999 | 318 | 121.858 | 8.175 | 318 | 122.487 | 8.303 |
| 319 | 123.305 | 8.245 | 319 | 123.345 | 8.254 | 319 | 123.852 | 8.418 | 319 | 123.651 | 8.614 |
| 321 | 121.188 | 8.119 | 321 | 121.326 | 8.11 | 321 | 121.612 | 8.243 | 320 | 122.774 | 8.317 |
| 322 | 118.03 | 7.95 | 322 | 118.027 | 7.942 | 322 | 118.56 | 8.081 | 322 | 118.938 | 8.229 |
| 323 | 120.267 | 7.96 | 323 | 120.355 | 7.963 | 323 | 120.718 | 8.113 | 323 | 121.793 | 8.345 |
| 324 | 123.387 | 8.165 | 324 | 123.716 | 8.155 | 324 | 123.699 | 8.309 | 324 | 125.596 | 8.45 |
| 325 | 122.007 | 8.044 | 325 | 122.188 | 8.064 | 325 | 122.353 | 8.196 | 325 | 123.648 | 8.379 |
| 326 | 121.953 | 8.044 | 326 | 122.102 | 8.053 | 326 | 122.235 | 8.174 | 326 | 123.286 | 8.357 |
| 327 | 118.046 | 8.056 | 327 | 118.172 | 8.06 | 327 | 118.454 | 8.173 | 327 | 119.514 | 8.364 |
| 328 | 123.073 | 8.049 | 328 | 123.359 | 8.06 | 328 | 123.326 | 8.175 | 328 | 125.344 | 8.392 |
| 329 | 121.132 | 7.914 | 329 | 121.333 | 7.941 | 329 | 121.43 | 8.029 | 329 | 123.189 | 8.315 |
| 330 | 119.77 | 7.834 | 330 | 119.94 | 7.851 | 330 | 120.147 | 7.948 | 330 | 121.683 | 8.269 |
| 331 | 119.119 | 8.039 | 331 | 119.408 | 8.063 | 331 | 119.407 | 8.166 | 331 | 121.429 | 8.524 |
| 332 | 115.416 | 8.104 | 332 | 115.662 | 8.13 | 332 | 115.801 | 8.245 | 332 | 117.278 | 8.485 |
| 333 | 117.15 | 8.113 | 333 | 117.207 | 8.128 | 333 | 117.443 | 8.233 | 333 | 117.904 | 8.433 |
| 334 | 122.383 | 8.028 | 334 | 122.45 | 8.027 | 334 | 122.664 | 8.145 | 334 | 123.006 | 8.266 |
| 335 | 109.23 | 8.167 | 335 | 109.443 | 8.163 | 335 | 109.5 | 8.288 | 335 | 110.274 | 8.325 |
| 336 | 119.571 | 8.041 | 336 | 119.593 | 8.033 | 336 | 119.723 | 8.161 | 336 | 119.828 | 8.231 |
| 337 | 119.686 | 8.26 | 337 | 119.933 | 8.257 | 337 | 119.947 | 8.396 | 337 | 121.145 | 8.554 |
| 338 | 109.007 | 8.257 | 338 | 109.141 | 8.262 | 338 | 109.29 | 8.372 | 338 | 109.949 | 8.472 |
| 339 | 119.635 | 8.041 | 339 | 119.636 | 8.037 | 339 | 119.882 | 8.166 | 339 | 119.99 | 8.29 |
| 340 | 122.258 | 8.147 | 340 | 122.307 | 8.144 | 340 | 122.621 | 8.304 | 340 | 123.692 | 8.46 |
| 341 | 124.021 | 8.191 | 341 | 124.21 | 8.205 | 341 | 124.406 | 8.352 | 341 | 125.407 | 8.505 |
| 342 | 113.746 | 8.079 | 342 | 113.855 | 8.083 | 342 | 114.059 | 8.225 | 342 | 114.989 | 8.37 |
| 343 | 121.388 | 8.194 | 343 | 121.485 | 8.192 | 343 | 121.634 | 8.315 | 343 | 122.191 | 8.493 |
| 344 | 120.283 | 8.228 | 344 | 120.366 | 8.227 | 344 | 120.538 | 8.341 | 344 | 121.166 | 8.471 |
| 345 | 119.228 | 8.396 | 345 | 119.435 | 8.399 | 345 | 119.532 | 8.541 | 345 | 120.225 | 8.633 |
| 346 | 120.631 | 8.352 | 346 | 120.691 | 8.342 | 346 | 120.915 | 8.492 | 346 | 121.254 | 8.563 |
| 347 | 116.606 | 8.337 | 347 | 116.635 | 8.326 | 347 | 116.886 | 8.469 | 347 | 117.082 | 8.498 |
| 348 | 110.451 | 8.187 | 348 | 110.448 | 8.179 | 348 | 110.62 | 8.318 | 348 | 110.457 | 8.352 |
| 350 | 115.829 | 8.443 | 350 | 115.89 | 8.42 | 350 | 116.206 | 8.604 | 349 | 116.451 | 8.621 |
| 351 | 110.352 | 8.322 | 351 | 110.361 | 8.319 | 351 | 110.591 | 8.451 | 351 | 110.784 | 8.571 |
| 352 | 118.509 | 8.281 | 352 | 118.549 | 8.289 | 352 | 118.627 | 8.41 | 352 | 118.689 | 8.445 |
| 353 | 119.058 | 8.432 | 353 | 119.139 | 8.424 | 353 | 119.315 | 8.571 | 353 | 119.691 | 8.624 |
| 354 | 120.017 | 8.362 | 354 | 120.122 | 8.347 | 354 | 120.213 | 8.492 | 354 | 120.463 | 8.512 |
| 355 | 119.027 | 8.426 | 355 | 119.277 | 8.381 | 355 | 119.247 | 8.557 | 355 | 119.625 | 8.581 |
| 356 | 120.037 | 8.358 | 356 | 120.287 | 8.321 | 356 | 120.317 | 8.477 | 356 | 120.524 | 8.502 |
| 357 | 109.207 | 8.408 | 357 | 109.247 | 8.388 | 357 | 109.463 | 8.527 | 357 | 109.485 | 8.505 |
| 358 | 118.515 | 8.271 | 358 | 118.483 | 8.252 | 358 | 118.631 | 8.388 | 358 | 118.767 | 8.442 |
| 359 | 120.373 | 8.284 | 359 | 120.389 | 8.281 | 359 | 120.613 | 8.421 | 359 | 120.987 | 8.497 |
| 360 | 121.215 | 8.329 | 360 | 121.126 | 8.314 | 360 | 121.51 | 8.466 | 360 | 121.912 | 8.547 |
| 361 | 122.319 | 8.286 | 361 | 122.179 | 8.263 | 361 | 122.742 | 8.443 | 361 | 123.112 | 8.556 |
| 362 | 123.155 | 8.416 | 362 | 122.379 | 8.352 | 362 | 123.5 | 8.572 | 362 | 122.83 | 8.621 |
| 364 | 117.837 | 8.47 | 364 | 117.945 | 8.422 | 364 | 118.318 | 8.636 | 364 | 119.036 | 8.642 |
| 365 | 120.584 | 8.209 | 365 | 120.532 | 8.207 | 365 | 120.939 | 8.366 | 365 | 121.17 | 8.48 |
| 366 | 124.736 | 8.222 | 366 | 124.759 | 8.199 | 366 | 125.054 | 8.369 | 366 | 125.247 | 8.389 |
| 367 | 119.285 | 8.141 | 367 | 119.359 | 8.126 | 367 | 119.716 | 8.308 | 367 | 119.937 | 8.34 |
| 368 | 110.616 | 8.253 | 368 | 110.673 | 8.259 | 368 | 110.997 | 8.392 | 368 | 110.909 | 8.428 |
| 369 | 115.508 | 8.214 | 369 | 115.517 | 8.209 | 369 | 115.707 | 8.342 | 369 | 115.672 | 8.365 |
| 370 | 110.658 | 8.46 | 370 | 110.671 | 8.444 | 370 | 110.84 | 8.593 | 370 | 110.578 | 8.47 |
| 371 | 118.496 | 8.272 | 371 | 118.615 | 8.275 | 371 | 118.746 | 8.392 | 371 | 118.778 | 8.422 |
| 372 | 119.22 | 8.403 | 372 | 119.226 | 8.429 | 372 | 119.442 | 8.542 | 372 | 119.767 | 8.596 |
| 373 | 115.678 | 8.19 | 373 | 115.734 | 8.178 | 373 | 115.921 | 8.319 | 373 | 116.169 | 8.366 |
| 374 | 121.963 | 8.179 | 374 | 122.005 | 8.183 | 374 | 122.245 | 8.319 | 374 | 122.493 | 8.379 |
| 375 | 117.815 | 8.2 | 375 | 117.841 | 8.194 | 375 | 118.199 | 8.34 | 375 | 118.406 | 8.393 |
| 376 | 110.348 | 7.863 | 376 | 110.368 | 7.85 | 376 | 110.558 | 7.929 | 376 | 110.483 | 7.881 |
| 377 | 115.372 | 8.178 | 377 | 115.376 | 8.179 | 377 | 115.482 | 8.313 | 377 | 115.346 | 8.329 |
| 378 | 120.732 | 8.481 | 378 | 120.697 | 8.49 | 378 | 120.998 | 8.621 | 378 | 121.259 | 8.68 |
| 379 | 116.008 | 8.263 | 379 | 116.033 | 8.258 | 379 | 116.273 | 8.391 | 379 | 116.4 | 8.424 |
| 380 | 110.697 | 8.365 | 380 | 110.753 | 8.362 | 380 | 110.948 | 8.485 | 380 | 110.909 | 8.478 |
| 381 | 123.484 | 7.965 | 381 | 123.555 | 7.954 | 381 | 123.629 | 8.082 | 381 | 123.606 | 8.114 |
| 382 | 123.001 | 8.128 | 382 | 123.063 | 8.123 | 382 | 123.312 | 8.277 | 382 | 123.755 | 8.334 |
| 383 | 119.454 | 7.946 | 383 | 119.504 | 7.936 | 383 | 119.976 | 8.125 | 383 | 120.454 | 8.197 |
| 384 | 112.23 | 8.266 | 384 | 112.24 | 8.243 | 384 | 112.638 | 8.417 | 384 | 112.778 | 8.428 |
| 385 | 121.152 | 8.025 | 385 | 121.176 | 8.007 | 385 | 121.398 | 8.174 | 385 | 121.424 | 8.224 |
| 386 | 110.661 | 8.266 | 386 | 110.585 | 8.261 | 386 | 110.974 | 8.384 | 386 | 110.885 | 8.436 |
| 387 | 115.578 | 8.081 | 387 | 115.603 | 8.072 | 387 | 115.805 | 8.216 | 387 | 115.857 | 8.285 |
| 388 | 125.668 | 8.353 | 388 | 125.702 | 8.339 | 388 | 125.904 | 8.498 | 388 | 126.131 | 8.529 |
| 389 | 114.408 | 8.188 | 389 | 114.445 | 8.178 | 389 | 114.69 | 8.323 | 389 | 114.896 | 8.366 |
| 390 | 120.476 | 8.297 | 390 | 120.541 | 8.291 | 390 | 120.75 | 8.425 | 390 | 121.054 | 8.509 |
| 391 | 124.004 | 8.188 | 391 | 124.029 | 8.176 | 391 | 124.197 | 8.311 | 391 | 124.301 | 8.329 |
| 392 | 107.838 | 8.291 | 392 | 107.854 | 8.275 | 392 | 108.056 | 8.414 | 392 | 108.055 | 8.406 |
| 393 | 115.464 | 8.174 | 393 | 115.397 | 8.156 | 393 | 115.644 | 8.309 | 393 | 115.661 | 8.333 |
| 394 | 110.853 | 8.459 | 394 | 110.818 | 8.444 | 394 | 111.143 | 8.593 | 394 | 111.115 | 8.587 |
| 395 | 115.516 | 8.222 | 395 | 115.512 | 8.196 | 395 | 115.727 | 8.362 | 395 | 115.674 | 8.371 |
| 396 | 110.472 | 8.378 | 396 | 110.539 | 8.366 | 396 | 110.659 | 8.513 | 396 | 110.729 | 8.519 |
| 397 | 120.223 | 8.11 | 397 | 120.117 | 8.1 | 397 | 120.477 | 8.245 | 397 | 120.58 | 8.294 |
| 398 | 121.471 | 8.415 | 398 | 121.468 | 8.4 | 398 | 121.851 | 8.564 | 398 | 122.18 | 8.608 |
| 399 | 108.482 | 7.788 | 399 | 108.498 | 7.765 | 399 | 108.622 | 7.875 | 399 | 108.715 | 7.798 |
| 400 | 108.272 | 8.106 | 400 | 108.182 | 8.036 | 400 | 108.238 | 8.135 | 400 | 108.323 | 8.189 |
| 401 | 119.905 | 8.117 | 401 | 119.817 | 8.119 | 401 | 120.092 | 8.256 | 401 | 120.15 | 8.303 |
| 402 | 110.711 | 8.371 | 402 | 110.479 | 8.374 | 402 | 111.02 | 8.507 | 402 | 110.847 | 8.502 |
| 403 | 115.498 | 8.173 | 403 | 115.517 | 8.14 | 403 | 115.768 | 8.307 | 403 | 115.686 | 8.306 |
| 404 | 117.557 | 8.397 | 404 | 117.642 | 8.387 | 404 | 117.889 | 8.549 | 404 | 118.213 | 8.596 |
| 405 | 121.706 | 8.351 | 405 | 121.551 | 8.303 | 405 | 121.922 | 8.472 | 405 | 121.995 | 8.476 |
| 406 | 120.945 | 8.2 | 406 | 120.178 | 8.243 | 406 | 121.174 | 8.307 | 406 | 119.924 | 8.499 |
| 407 | 116.564 | 8.209 | 407 | 116.349 | 8.162 | 407 | 116.806 | 8.329 | 407 | 116.807 | 8.369 |
| 408 | 122.508 | 8.28 | 408 | 122.67 | 8.257 | 408 | 122.776 | 8.404 | 408 | 123.296 | 8.461 |
| 409 | 116.07 | 8.173 | 409 | 116.158 | 8.171 | 409 | 116.393 | 8.298 | 409 | 116.898 | 8.433 |
| 410 | 117.426 | 8.255 | 410 | 117.472 | 8.244 | 410 | 117.79 | 8.41 | 410 | 117.913 | 8.47 |
| 411 | 110.234 | 8.27 | 411 | 110.282 | 8.255 | 411 | 110.505 | 8.404 | 411 | 110.437 | 8.407 |
| 412 | 120.858 | 8.002 | 412 | 121.007 | 7.997 | 412 | 121.117 | 8.12 | 412 | 121.236 | 8.187 |
| 413 | 111.395 | 8.226 | 413 | 111.243 | 8.204 | 413 | 111.798 | 8.356 | 413 | 111.038 | 8.406 |
| 414 | 124.562 | 7.635 | 414 | 123.272 | 7.705 | 414 | 124.642 | 7.757 | 414 | 120.033 | 8.143 |

Table S3. 1H, 15N chemical shifts from this research.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **TDP-43 LCD** | **pH5.5 20mM MES**  **(70 μM)** | | **pH6.0 10mM PB (1h)**  **(100 μM)** | | **pH6.0 10 mM PB (22h)**  **(100 μM)** | | **pH6.0 10 mM PB+20ng/mL RNA**  **(100 μM)** | | **pH6.0 10 mM PB+150 mM Urea**  **(100 μM)** | |
| 15N | 1H | 15N | 1H | 15N | 1H | 15N | 1H | 15N | 1H |
| 269 | 121.19 | 8.4 | 121.04 | 8.41 | 121.09 | 8.41 | 121.04 | 8.41 | 121.04 | 8.41 |
| 270 | 122.85 | 8.18 | 122.76 | 8.17 | 122.79 | 8.17 | 122.76 | 8.17 | 122.78 | 8.17 |
| 271 | 121.77 | 8.3 | 121.7 | 8.3 | 121.7 | 8.3 | 121.7 | 8.3 | 121.71 | 8.31 |
| 272 | 121.82 | 8.35 | 121.82 | 8.35 | 121.82 | 8.35 | 121.82 | 8.35 | 121.84 | 8.36 |
| 273 | 116.46 | 8.29 | 116.37 | 8.28 | 116.37 | 8.28 | 116.37 | 8.28 | 116.4 | 8.29 |
| 274 | 110.48 | 8.38 | 110.48 | 8.38 | 110.48 | 8.38 | 110.48 | 8.39 | 110.52 | 8.39 |
| 275 | 120.39 | 8.08 | 120.38 | 8.08 | 120.38 | 8.08 | 120.38 | 8.08 | 120.41 | 8.08 |
| 276 | 120.86 | 8.32 | 120.86 | 8.32 | 120.86 | 8.32 | 120.86 | 8.32 | 120.88 | 8.33 |
| 277 | 110.72 | 8.27 | 110.72 | 8.27 | 110.72 | 8.27 | 110.72 | 8.27 | 110.76 | 8.27 |
| 278 | 107.87 | 7.9 | 107.87 | 7.9 | 107.87 | 7.9 | 107.87 | 7.9 | 107.9 | 7.91 |
| 279 | 119.05 | 8.33 | 119.05 | 8.33 | 119.07 | 8.34 | 119.07 | 8.34 | 119.07 | 8.35 |
| 281 | 108.67 | 8.39 | 108.67 | 8.39 | 108.67 | 8.39 | 108.68 | 8.39 | 108.7 | 8.39 |
| 282 | 108.18 | 8.04 | 108.19 | 8.04 | 108.19 | 8.04 | 108.19 | 8.04 | 108.22 | 8.05 |
| 283 | 119.7 | 8.14 | 119.76 | 8.13 | 119.76 | 8.13 | 119.77 | 8.14 | 119.79 | 8.14 |
| 284 | 110.28 | 8.39 | 110.28 | 8.39 | 110.28 | 8.39 | 110.32 | 8.4 | 110.35 | 8.4 |
| 285 | 118.63 | 8.27 | 118.63 | 8.27 | 118.63 | 8.27 | 118.63 | 8.27 | 118.65 | 8.28 |
| 286 | 120.46 | 8.45 | 120.46 | 8.45 | 120.46 | 8.45 | 120.48 | 8.46 | 120.5 | 8.46 |
| 287 | 109.44 | 8.38 | 109.44 | 8.38 | 109.44 | 8.38 | 109.46 | 8.38 | 109.49 | 8.38 |
| 288 | 108.15 | 8.03 | 108.15 | 8.03 | 108.17 | 8.04 | 108.15 | 8.03 | 108.18 | 8.04 |
| 289 | 119.69 | 8.14 | 119.69 | 8.14 | 119.73 | 8.14 | 119.7 | 8.15 | 119.72 | 8.15 |
| 290 | 110.29 | 8.4 | 110.29 | 8.4 | 110.29 | 8.4 | 110.3 | 8.4 | 110.33 | 8.41 |
| 291 | 118.57 | 8.27 | 118.57 | 8.27 | 118.57 | 8.27 | 118.57 | 8.27 | 118.59 | 8.28 |
| 292 | 116.2 | 8.31 | 116.2 | 8.31 | 116.2 | 8.31 | 116.22 | 8.32 | 116.23 | 8.32 |
| 293 | 122.43 | 8.37 | 122.43 | 8.37 | 122.43 | 8.37 | 122.48 | 8.38 | 122.5 | 8.38 |
| 294 | 109.5 | 8.32 | 109.49 | 8.33 | 109.49 | 8.33 | 109.49 | 8.33 | 109.53 | 8.33 |
| 295 | 108.63 | 8.26 | 108.63 | 8.26 | 108.63 | 8.26 | 108.66 | 8.26 | 108.66 | 8.26 |
| 296 | 108.55 | 8.27 | 108.59 | 8.27 | 108.59 | 8.27 | 108.6 | 8.27 | 108.62 | 8.27 |
| 297 | 123.62 | 8.23 | 123.67 | 8.23 | 123.67 | 8.23 | 123.67 | 8.24 | 123.68 | 8.24 |
| 298 | 107.99 | 8.36 | 107.99 | 8.36 | 107.99 | 8.36 | 107.99 | 8.36 | 108.02 | 8.36 |
| 299 | 121.27 | 8.1 | 121.27 | 8.1 | 121.31 | 8.1 | 121.31 | 8.1 | 121.31 | 8.1 |
| 300 | 109.16 | 8.41 | 109.16 | 8.41 | 109.16 | 8.41 | 109.16 | 8.41 | 109.17 | 8.42 |
| 301 | 118.55 | 8.27 | 118.55 | 8.27 | 118.55 | 8.27 | 118.55 | 8.27 | 118.55 | 8.28 |
| 302 | 119.04 | 8.46 | 119.04 | 8.46 | 119.04 | 8.46 | 119.07 | 8.46 | 119.08 | 8.47 |
| 303 | 120.38 | 8.33 | 120.38 | 8.33 | 120.38 | 8.33 | 120.38 | 8.33 | 120.43 | 8.34 |
| 304 | 109.51 | 8.39 | 109.51 | 8.39 | 109.51 | 8.39 | 109.51 | 8.39 | 109.51 | 8.39 |
| 305 | 115.45 | 8.18 | 115.45 | 8.18 | 115.45 | 8.18 | 115.45 | 8.18 | 115.44 | 8.18 |
| 306 | 120.42 | 8.49 | 120.48 | 8.49 | 120.48 | 8.49 | 120.46 | 8.5 | 120.49 | 8.5 |
| 307 | 120.33 | 8.3 | 120.33 | 8.3 | 120.33 | 8.3 | 120.33 | 8.3 | 120.37 | 8.31 |
| 308 | 109.54 | 8.37 | 109.54 | 8.37 | 109.54 | 8.37 | 109.54 | 8.38 | 109.55 | 8.38 |
| 309 | 108.63 | 8.23 | 108.63 | 8.23 | 108.63 | 8.23 | 108.62 | 8.24 | 108.65 | 8.24 |
| 310 | 108.8 | 8.29 | 108.82 | 8.29 | 108.82 | 8.29 | 108.82 | 8.3 | 108.83 | 8.3 |
| 311 | 119.35 | 8.17 | 119.4 | 8.17 | 119.4 | 8.17 | 119.38 | 8.18 | 119.41 | 8.18 |
| 312 | 119.42 | 8.31 | 119.42 | 8.31 | 119.42 | 8.31 | 119.42 | 8.32 | 119.46 | 8.32 |
| 313 | 120.9 | 8.21 | 120.9 | 8.21 | 120.9 | 8.21 | 120.89 | 8.21 | 120.93 | 8.22 |
| 314 | 109.89 | 8.28 | 109.84 | 8.28 | 109.89 | 8.28 | 109.91 | 8.28 | 109.9 | 8.29 |
| 315 | 123.61 | 8 | 123.61 | 8 | 123.61 | 8 | 123.61 | 8 | 123.63 | 8 |
| 316 | 118.14 | 8.03 | 118.09 | 8.01 | 118.14 | 8.02 | 118.15 | 8.02 | 118.17 | 8.03 |
| 317 | 116.57 | 8.01 | 116.57 | 8.01 | 116.61 | 8.02 | 116.61 | 8.01 | 116.64 | 8.02 |
| 318 | 121.37 | 7.99 | 121.35 | 7.98 | 121.35 | 7.98 | 121.38 | 7.99 | 121.42 | 8 |
| 319 | 123.34 | 8.24 | 123.36 | 8.22 | 123.35 | 8.23 | 123.39 | 8.24 | 123.4 | 8.25 |
| 321 | 121.24 | 8.12 | 121.19 | 8.12 | 121.23 | 8.12 | 121.22 | 8.12 | 121.27 | 8.12 |
| 322 | 118.09 | 7.95 | 118.05 | 7.95 | 118.09 | 7.95 | 118.1 | 7.95 | 118.12 | 7.96 |
| 323 | 120.3 | 7.96 | 120.18 | 7.95 | 120.29 | 7.96 | 120.3 | 7.96 | 120.3 | 7.96 |
| 324 | 123.34 | 8.17 | 123.22 | 8.16 | 123.34 | 8.16 | 123.33 | 8.17 | 123.36 | 8.17 |
| 325 | 122.01 | 8.04 | 121.99 | 8.03 | 122.02 | 8.04 | 122.03 | 8.04 | 121.99 | 8.03 |
| 326 | 121.95 | 8.04 | 121.94 | 8.05 | 121.94 | 8.05 | 121.97 | 8.05 | 121.94 | 8.05 |
| 327 | 118.05 | 8.06 | 117.99 | 8.07 | 118.04 | 8.06 | 118.06 | 8.06 | 118.08 | 8.07 |
| 328 | 122.99 | 8.04 | 122.91 | 8.04 | 123.04 | 8.05 | 123 | 8.04 | 123.06 | 8.05 |
| 329 | 121.14 | 7.91 | 121.14 | 7.92 | 121.15 | 7.91 | 121.14 | 7.91 | 121.19 | 7.92 |
| 330 | 119.77 | 7.83 | 119.77 | 7.85 | 119.78 | 7.84 | 119.78 | 7.83 | 119.84 | 7.85 |
| 331 | 119.12 | 8.04 | 119.01 | 8.04 | 119.13 | 8.04 | 119.12 | 8.03 | 119.15 | 8.04 |
| 332 | 115.44 | 8.09 | 115.38 | 8.09 | 115.44 | 8.1 | 115.43 | 8.1 | 115.46 | 8.11 |
| 333 | 117.18 | 8.11 | 117.18 | 8.11 | 117.18 | 8.11 | 117.18 | 8.11 | 117.21 | 8.12 |
| 334 | 122.43 | 8.03 | 122.42 | 8.03 | 122.43 | 8.03 | 122.44 | 8.03 | 122.42 | 8.03 |
| 335 | 109.23 | 8.17 | 109.17 | 8.17 | 109.25 | 8.17 | 109.26 | 8.17 | 109.26 | 8.17 |
| 336 | 119.57 | 8.04 | 119.59 | 8.04 | 119.61 | 8.04 | 119.59 | 8.04 | 119.61 | 8.04 |
| 337 | 119.7 | 8.26 | 119.61 | 8.24 | 119.72 | 8.25 | 119.69 | 8.26 | 119.73 | 8.26 |
| 338 | 108.96 | 8.25 | 108.88 | 8.25 | 108.96 | 8.25 | 108.97 | 8.25 | 108.98 | 8.26 |
| 339 | 119.64 | 8.04 | 119.67 | 8.04 | 119.68 | 8.04 | 119.66 | 8.04 | 119.67 | 8.04 |
| 340 | 122.26 | 8.15 | 122.17 | 8.14 | 122.28 | 8.14 | 122.27 | 8.15 | 122.3 | 8.15 |
| 341 | 124.02 | 8.19 | 124.01 | 8.19 | 124.07 | 8.19 | 124.07 | 8.19 | 124.09 | 8.2 |
| 342 | 113.76 | 8.08 | 113.76 | 8.08 | 113.8 | 8.08 | 113.78 | 8.08 | 113.81 | 8.08 |
| 343 | 121.4 | 8.19 | 121.4 | 8.19 | 121.43 | 8.19 | 121.4 | 8.19 | 121.44 | 8.2 |
| 344 | 120.27 | 8.22 | 120.27 | 8.22 | 120.3 | 8.23 | 120.31 | 8.22 | 120.33 | 8.23 |
| 345 | 119.23 | 8.4 | 119.23 | 8.4 | 119.28 | 8.4 | 119.23 | 8.4 | 119.27 | 8.4 |
| 346 | 120.63 | 8.35 | 120.63 | 8.35 | 120.63 | 8.35 | 120.63 | 8.35 | 120.69 | 8.36 |
| 347 | 116.63 | 8.33 | 116.63 | 8.33 | 116.63 | 8.33 | 116.65 | 8.34 | 116.67 | 8.34 |
| 348 | 110.49 | 8.19 | 110.49 | 8.19 | 110.49 | 8.19 | 110.49 | 8.19 | 110.51 | 8.19 |
| 350 | 115.88 | 8.45 | 115.88 | 8.45 | 115.88 | 8.45 | 115.9 | 8.45 | 115.91 | 8.45 |
| 351 | 110.35 | 8.32 | 110.35 | 8.32 | 110.39 | 8.32 | 110.4 | 8.32 | 110.41 | 8.33 |
| 352 | 118.51 | 8.28 | 118.51 | 8.28 | 118.51 | 8.28 | 118.51 | 8.28 | 118.55 | 8.29 |
| 353 | 119.1 | 8.43 | 119.1 | 8.43 | 119.1 | 8.43 | 119.1 | 8.43 | 119.12 | 8.44 |
| 354 | 120.02 | 8.36 | 120.02 | 8.36 | 120.02 | 8.36 | 120.02 | 8.36 | 120.04 | 8.37 |
| 355 | 119.06 | 8.43 | 119.06 | 8.43 | 119.06 | 8.43 | 119.06 | 8.43 | 119.09 | 8.43 |
| 356 | 120.06 | 8.35 | 120.06 | 8.35 | 120.06 | 8.35 | 120.06 | 8.35 | 120.08 | 8.36 |
| 357 | 109.21 | 8.41 | 109.21 | 8.41 | 109.21 | 8.41 | 109.22 | 8.41 | 109.23 | 8.42 |
| 358 | 118.52 | 8.27 | 118.52 | 8.27 | 118.52 | 8.27 | 118.52 | 8.27 | 118.52 | 8.27 |
| 359 | 120.37 | 8.28 | 120.37 | 8.28 | 120.37 | 8.28 | 120.37 | 8.28 | 120.41 | 8.29 |
| 360 | 121.14 | 8.32 | 121.22 | 8.33 | 121.22 | 8.33 | 121.22 | 8.33 | 121.27 | 8.33 |
| 361 | 122.32 | 8.29 | 122.32 | 8.29 | 122.32 | 8.29 | 122.41 | 8.28 | 122.42 | 8.29 |
| 362 | 123.09 | 8.41 | 123.14 | 8.41 | 123.14 | 8.41 | 123.14 | 8.41 | 123.21 | 8.42 |
| 364 | 117.88 | 8.48 | 117.86 | 8.47 | 117.86 | 8.47 | 117.89 | 8.48 | 117.93 | 8.48 |
| 365 | 120.58 | 8.21 | 120.58 | 8.21 | 120.69 | 8.21 | 120.65 | 8.21 | 120.68 | 8.22 |
| 366 | 124.74 | 8.22 | 124.73 | 8.22 | 124.77 | 8.22 | 124.76 | 8.22 | 124.8 | 8.23 |
| 367 | 119.32 | 8.14 | 119.28 | 8.14 | 119.32 | 8.14 | 119.32 | 8.15 | 119.35 | 8.15 |
| 368 | 110.62 | 8.25 | 110.62 | 8.25 | 110.62 | 8.25 | 110.62 | 8.25 | 110.64 | 8.26 |
| 369 | 115.53 | 8.21 | 115.53 | 8.21 | 115.53 | 8.21 | 115.53 | 8.21 | 115.56 | 8.22 |
| 370 | 110.63 | 8.46 | 110.63 | 8.46 | 110.63 | 8.46 | 110.65 | 8.47 | 110.65 | 8.47 |
| 371 | 118.5 | 8.27 | 118.5 | 8.27 | 118.5 | 8.27 | 118.5 | 8.27 | 118.53 | 8.28 |
| 372 | 119.26 | 8.4 | 119.26 | 8.4 | 119.26 | 8.4 | 119.27 | 8.41 | 119.3 | 8.41 |
| 373 | 115.69 | 8.19 | 115.69 | 8.19 | 115.69 | 8.19 | 115.69 | 8.19 | 115.67 | 8.19 |
| 374 | 121.96 | 8.18 | 121.96 | 8.18 | 121.96 | 8.18 | 121.96 | 8.18 | 121.99 | 8.19 |
| 375 | 117.84 | 8.2 | 117.84 | 8.2 | 117.88 | 8.2 | 117.88 | 8.2 | 117.89 | 8.21 |
| 376 | 110.4 | 7.86 | 110.38 | 7.87 | 110.38 | 7.87 | 110.41 | 7.86 | 110.42 | 7.87 |
| 377 | 115.37 | 8.18 | 115.37 | 8.18 | 115.37 | 8.18 | 115.38 | 8.18 | 115.38 | 8.18 |
| 378 | 120.73 | 8.48 | 120.78 | 8.49 | 120.78 | 8.49 | 120.78 | 8.49 | 120.8 | 8.49 |
| 379 | 116.05 | 8.26 | 116.05 | 8.26 | 116.05 | 8.26 | 116.06 | 8.26 | 116.07 | 8.27 |
| 380 | 110.7 | 8.37 | 110.7 | 8.37 | 110.7 | 8.37 | 110.75 | 8.37 | 110.73 | 8.37 |
| 381 | 123.48 | 7.97 | 123.48 | 7.97 | 123.53 | 7.97 | 123.5 | 7.97 | 123.53 | 7.97 |
| 382 | 123 | 8.13 | 122.99 | 8.12 | 123.01 | 8.13 | 123.02 | 8.13 | 123.06 | 8.13 |
| 383 | 119.45 | 7.94 | 119.43 | 7.94 | 119.47 | 7.94 | 119.49 | 7.95 | 119.51 | 7.95 |
| 384 | 112.23 | 8.27 | 112.22 | 8.26 | 112.22 | 8.26 | 112.25 | 8.27 | 112.27 | 8.27 |
| 385 | 121.16 | 8.03 | 121.17 | 8.02 | 121.17 | 8.02 | 121.19 | 8.03 | 121.21 | 8.03 |
| 386 | 110.67 | 8.26 | 110.67 | 8.26 | 110.67 | 8.26 | 110.67 | 8.26 | 110.7 | 8.27 |
| 387 | 115.58 | 8.08 | 115.58 | 8.08 | 115.58 | 8.08 | 115.6 | 8.09 | 115.63 | 8.09 |
| 388 | 125.67 | 8.35 | 125.67 | 8.35 | 125.71 | 8.35 | 125.71 | 8.36 | 125.72 | 8.36 |
| 389 | 114.44 | 8.19 | 114.44 | 8.19 | 114.44 | 8.19 | 114.43 | 8.19 | 114.48 | 8.19 |
| 390 | 120.43 | 8.29 | 120.43 | 8.29 | 120.43 | 8.29 | 120.43 | 8.29 | 120.45 | 8.3 |
| 391 | 124 | 8.19 | 123.97 | 8.18 | 124.01 | 8.19 | 124.01 | 8.19 | 124.03 | 8.19 |
| 392 | 107.85 | 8.29 | 107.85 | 8.29 | 107.85 | 8.29 | 107.89 | 8.29 | 107.91 | 8.29 |
| 393 | 115.5 | 8.17 | 115.5 | 8.17 | 115.5 | 8.17 | 115.52 | 8.18 | 115.49 | 8.18 |
| 394 | 110.9 | 8.46 | 110.9 | 8.46 | 110.91 | 8.46 | 110.92 | 8.47 | 110.93 | 8.47 |
| 395 | 115.55 | 8.22 | 115.55 | 8.22 | 115.55 | 8.22 | 115.55 | 8.22 | 115.58 | 8.23 |
| 396 | 110.53 | 8.38 | 110.53 | 8.38 | 110.53 | 8.38 | 110.54 | 8.38 | 110.56 | 8.38 |
| 397 | 120.22 | 8.11 | 120.22 | 8.11 | 120.27 | 8.11 | 120.22 | 8.11 | 120.27 | 8.12 |
| 398 | 121.42 | 8.41 | 121.49 | 8.41 | 121.49 | 8.41 | 121.51 | 8.42 | 121.52 | 8.42 |
| 399 | 108.48 | 7.79 | 108.51 | 7.79 | 108.51 | 7.79 | 108.52 | 7.79 | 108.51 | 7.79 |
| 400 | 108.31 | 8.1 | 108.31 | 8.11 | 108.31 | 8.11 | 108.34 | 8.11 | 108.34 | 8.11 |
| 401 | 119.87 | 8.12 | 119.87 | 8.12 | 119.91 | 8.12 | 119.87 | 8.12 | 119.92 | 8.13 |
| 402 | 110.71 | 8.37 | 110.71 | 8.37 | 110.71 | 8.37 | 110.71 | 8.37 | 110.74 | 8.38 |
| 403 | 115.56 | 8.17 | 115.56 | 8.17 | 115.56 | 8.17 | 115.57 | 8.18 | 115.57 | 8.18 |
| 404 | 117.6 | 8.4 | 117.6 | 8.4 | 117.6 | 8.4 | 117.61 | 8.4 | 117.62 | 8.4 |
| 405 | 121.75 | 8.35 | 121.75 | 8.35 | 121.75 | 8.35 | 121.75 | 8.35 | 121.78 | 8.36 |
| 406 | 120.95 | 8.2 | 120.95 | 8.2 | 120.98 | 8.2 | 120.96 | 8.2 | 120.99 | 8.21 |
| 407 | 116.56 | 8.21 | 116.56 | 8.21 | 116.56 | 8.21 | 116.6 | 8.21 | 116.62 | 8.21 |
| 408 | 122.51 | 8.28 | 122.51 | 8.28 | 122.51 | 8.28 | 122.51 | 8.28 | 122.5 | 8.29 |
| 409 | 116.05 | 8.17 | 116.09 | 8.17 | 116.09 | 8.17 | 116.12 | 8.17 | 116.14 | 8.18 |
| 410 | 117.46 | 8.25 | 117.44 | 8.25 | 117.49 | 8.25 | 117.47 | 8.26 | 117.5 | 8.26 |
| 411 | 110.31 | 8.27 | 110.31 | 8.27 | 110.31 | 8.27 | 110.33 | 8.27 | 110.33 | 8.27 |
| 412 | 120.88 | 8 | 120.88 | 8 | 120.93 | 8 | 120.91 | 8 | 120.93 | 8.01 |
| 413 | 111.34 | 8.23 | 111.39 | 8.22 | 111.39 | 8.22 | 111.45 | 8.23 | 111.45 | 8.23 |
| 414 | 124.53 | 7.65 | 124.57 | 7.64 | 124.57 | 7.64 | 124.57 | 7.64 | 124.6 | 7.64 |

Movie S1 (separate file). DIC movie of 100 μM TDP-43 LCD in pH 6.0 10 mM phosphate buffer.

Movie S2 (separate file). Optical tweezer-controlled fusion of two TDP-43 LCD droplets in pH 6.0 10 mM phosphate buffer at 100 μM.

Movie S3a (separate file). DIC movie of 200 μM TDP-43 LCD in pH 6.0 10 mM phosphate buffer.

Movie S3b (separate file). The dilution process from 200 μM of TDP-43 LCD to 100 μM in pH 6.0 10 mM phosphate buffer. An equal volume of blank phosphate buffer was added to 200 μM of TDP-43 LCD solution after 1 minute filming. A continuous change of droplet sizes and density could be observed indicating the blank buffer was slowly diffusing into the solution.

Movie S4 (separate file). DIC movie of 20 μM TDP-43 LCD in pH 6.0 10 mM phosphate buffer.

Movie S5 (separate file). DIC movie of 40 μM TDP-43 LCD in pH 6.0 10 mM phosphate buffer.

Movie S6a (separate file). DIC movie of 100 μM TDP-43 LCD in pH 6.0 10 mM phosphate buffer with yeast RNA (20ng/μL).

Movie S6b (separate file). The process of adding yeast RNA (500ng/μL) to 100 μM TDP-43 LCD in pH 6.0 10 mM phosphate buffer to a final concentration of 20ng/μL was observed by DIC. Yeast RNA was added at 21 second, but a clear change of droplet sizes was observed only after 3 min 33 second.

Movie S7 (separate file). DIC movie of 40 μM TDP-43 LCD in pH 6.0 10 mM phosphate buffer with yeast RNA (20ng/μL).

Movie S8 (separate file). DIC movie of 70 μM TDP-43 LCD in pH 5.5 20 mM MES buffer.

Movie S9 (separate file). DIC movie of 100 μM TDP-43 LCD in pH 6.0 10 mM phosphate buffer with 150mM urea.

Movie S10 (separate file). DIC movie of 100 μM TDP-16E in pH 6.0 10 mM phosphate buffer with yeast RNA (20ng/μL).