Supplementary Table 1: Data summary of main findings in the different model systems

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|  | **ER-Mito Association**  | **CCh [Ca2+]cyto vs [Ca2+]mito** | **SOCE [Ca2+]cyto vs [Ca2+]mito** |
| WT | - | - | - |
| *Opa1-/-* | Increased | Leftward shift | Rightward shift |
| *Opa1-/-* + OPA1 | Rescued | Partial rescue | Rescued |
| **ADOA Patients’ cell** |
| Control | - | - | ND |
| c.870+5g>a | Increased | Partial leftward Shift  | ND |
| c.889c>t | Increased | Partial leftward Shift | ND |
| c.2713c>t | Unchanged | Partial leftward Shift | ND |
| c.2818+5g>a | Increased | ND | ND |
| **OPA1 mutants’ rescue (*Opa1-/-* background)** |
| *Opa1-/-* | Increased | Leftward shift | Rightward shift |
| +OPA1 WT | Rescued | Partial rescue | Rescued |
| c.870+5g>a | ND | Partial rescue | Rescued |
| c.889c>t | ND | Partial rescue | Rescued |
| c.1334g>a | ND | Partial rescue | Rescued |
| c.2708delTTAG | ND | Not rescued | Rescued |
| c.2713c>t | ND | Not rescued | Rescued |
| c.2818+5g>a | ND | Not rescued | Rescued |
| **OPA1 mutants’ overexpression (WT background)** |
| WT | - | - | - |
| +OPA1 WT | ND | Unchanged | ND |
| c.870+5g>a | ND | Leftward shift | ND |
| c.889c>t | ND | Unchanged  | ND |
| c.1334g>a | ND | Leftward shift | ND |
| c.2708delTTAG | ND | Leftward shift | ND |
| c.2713c>t | ND | Unchanged | ND |
| c.2818+5g>a | ND | Leftward shift | ND |

ND: not determined