Supporting Information for

Thermoring-driven allosteric gating coupling in TRPV2

Running title: Thermoring-coded TRPV2

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This supplementary material includes:

Tables S1, S2, S3 and S4.

Table S1. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 1 PE-bound closed rTRPV2$_{STD}$ subunit reconstituted in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID, 11ID-B).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	K300-E352, K380-E708, R371-D655
H-bond	<3.9 Å donor-H-acceptor <60°	A257-K307, I256/D258-N263, D258-S264, G306-N368, D272-H313, R280-Y323, E288-R317-L326/R328/K329, N292-Q294/L296, G295-N354-K300, A303/K304-C364, E309-R312, Q316-E376, F319-S327-Q324, P325/S327-R702, R328-D344/S346, E332-R706, Y343-E709, D344-S346/R702, S347-V356, D349-K385/E685, S350-K385/E672, E358-R459, C364-S366-N368, R369-E469, E376-N379, K380-E384/R706, Q383-D387, K385-E672, R388-E685, N396-Y675, Y400-N511, T408-W509, Q414-H438-Y447-W677, Q452-E473, W457-R460, R458-E670-R459, L475-N511, Q479-S504, T483-Q487, Y497-Q414, Y514-R517, T516-T522/S526, R517-W660, T522-S526-Q530, Y544-Y629-L600/T604, Y590-E599, F603-G606, S646-E647, N673-K682, R694-D700-R702
π–π interaction	2.65–6.5 Å	F362-F462, W386-F393-F394/Y514/Y515, F394-F397-Y515, F394-F519, Y400-Y403, Y400-F476, Y400-Y515, Y403-F407, Y412-H413, Y447-W676, Y455-F456/F462, F467-Y471, Y471-F472-F476-Y514/Y515, Y514-Y515, F472-Y514, Y544-F601, F547-F551-Y629, W657-W660, W676-W677-Y675, W712-W715
cation–π interaction	<6.0 Å	W351-R684-W703, F362-R459, H438-R490
CH_3/CH–π interaction	2.65-3.01 Å	Y271-I314, I268-H313, Q276-Y323, F330-V691, W333-V340, P337-W712/W715, Y343-P377, A361-F362, H370-I659, L381-F705, W386- K664, M404-W509, F405-V409, F407-I441/L505, L450-W676, W454-R458, R490-Y497, V543-F547-L632, Y544-L548, F549-V553, L555-Y590, F603-L610-F612, , R617-F618, W657-K661, W660-K664, L688-W703, W715-L719
Lone pair–π interaction	3-3.7 Å	F395-C399, Y629-T633

Table S2. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in 2 PE-bound inactivated rTRPV2$_{STD}$ subunit reconstituted in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID, 11ID-A).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	E309-R312, E288-R328, K380-E708, K531/R535-E647, D344-R702, D536-R539
H-bond	<3.9 Å donor-H-acceptor <60°	A257-K307, D258-N263, N259-G306, D272-H313, R280-Y323, T284-Q286, E288-R317-L326/R328/K329, N292-Q294/L296, G295-N354, K300-E352, A303/K304-C364, Q316-E376, E318-T331/K329, F319-S327-Q324, P325/S327-R702, T331-R339, E332-R706, S341/Y343-E709, S347-V356, D349-K385/E685, E358-R459, S361-R369, N368-R371-D655, R369-D469, V374-N379, N379-K661, K380-R706, Q383-D387, E384-R388-E685, K385-E672/E685, N396-Y675, Y400/Y403-Q479, Y400-G508, T408-W509, Q414-H438-Q487, Y447-W677, Y455-E670, R459-N673, S466-S470, L475-N511, Y471-PE-Q530, Q479-T483, S486-Y497, Y514-S667, R517-W660, H521-G523/S656, T522-S526, R535-D536, Y544-Y629-T604, S559-Y590, F603-G606, E609-L610, L616-R619, K681-K682, R694-D700-R702, N711-A714, W715-T718
π–π interaction	2.65–6.5 Å	F362-F462, W386-F393-F394/Y514/Y515, F394-F397-Y515, Y400-Y403, Y400-F476, Y400-Y515, Y403-F407, Y412-H413, Y447-W676, F467-Y471, F476-Y514/Y515, Y514-Y515, H521-W660, Y455-F456, F472-Y514, F540-Y544, Y544-F601, F551-Y629, W657-W660, W676-W677, W712-W715
cation–π interaction	<6.0 Å	W351-R684-W703, F362-R459, H438-R490, W454-R458, W457-R460, W660-K664
CH_3/CH–π interaction	2.65-3.01 Å	Y271-I314, I268-H313, Q276-Y323, F330-V691, W333-V340, P337-W712/W715, H370-I659, W386-V390/K664, M404-W509, F405-V409, F407-I441, V410-H438, L450-W676, R490-Y497, F456-L477, F547-L632, F549-V553, L555-Y590, F603-L610, W657-K661, L688-W703, W715-L719
Lone pair–π interaction	3-3.7 Å	F395-C399, Y629-T633

Table S3. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V253 to P725 in each subunit of 1 PE-bound inactivated hTRPV2 reconstituted in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID, 11HZ).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	E308-R311, K327-E708, R337-E708, E350-R683, R367-D467, R369-D655, R456-E670, R457-D467, E471-R515, D534-R537, E599-K602, K693-D695
H-bond	<3.9 Å donor-H-acceptor <60°	V253-S256, M254/S256-K306, I255/D257-M262, D257-S259, D271-H312, E287-R316, R290-D294, N291-L295, T296-K299-S345, A302/K303/E304-C362, Q315-E374, R316-L324, F318-L321/S325, L321-S325, H323/S325-R701, R326-A344, K327-Y341, T329-L721, E330-R705/C722, C332-Y333/G334, S339-E708, D342-R701, S345-E350, D347-S353/K383/A684, S348-E672, S364-H366, Q381-D385, K383-S348/E672, K390-N394, N398-Y513, T406-W507, A407-H411, Q412-H436-Q485, Y453-R457, I466-K529, D467-Q663, T468-E471/R515, Q477-N509, T514-T520/S524, R515-W660, D534-T648, Y542-Y629/T604, L600-Y629, R679-N673/G674, D699-R701, N710-A712, T720-C722
π–π interaction	2.65–6.5 Å	Y270-H312, H361-H458, W384-F391-Y513, F392-F395, F395-Y513, F403-W507, Y410-H411, H436-F489, Y445-Y675/W676, W452-Y675, Y453-F454, F465-Y469, Y469-F470-Y512, F474-Y512, Y512-Y513, Y542-F601, F545-F549, F549-Y629, F603-Y629, H617-F618, W657-W660, W711-W714
cation–π interaction	<6.0 Å	R683-W702
CH_3/CH–π interaction	2.65-3.01 Å	V266-H312, Q275-F318, F310-L314, H323-L324, F328-V690, W331-V338/P725, P335-W711, Y341-P375, W384-K664, M402-W507, Q518-W660,Y523-I527, F538-L641/Y542, F545-L637, F547-V551, W657-K661, M687-W702
Lone pair–π interaction	3-3.7 Å	Y629-T633

Table S4. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V253 to P725 in each subunit of 1 PE-bound inactivated hTRPV2$_{HDN}$ reconstituted in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID, 11IA).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	D347-E672, E350-K683, D534-R537
H-bond	<3.9 Å donor-H-acceptor <60°	V253-S256, M254/S256-K306, I255/D257-S259-E261, D257-N262, Y270-E287, D271-H312, E287-R316, N291-L295, A302/K303/E304-C362, E308-R311, Q315-E374, R316-L324, F318-S325, R326-D342/A344, K327-Y341, E330-R705, C332-G334/V336, S339-E708, D342/A344-R701, S345-V354, D347-S353/K383/A684, S348-E672, D347-C349-E350/K681, E350-S353, A359-R367-D467, S364-H366, H368-S658, Q381-K661/K664, K383-S348/E672, N394-W677, N398-Y513, Y401-I439, T406-W507, Q412-H436-L432, Y445-Y675, Q450-E471, W455-H458, R456-E670, R457-D467-Q663, L473/Q477-N509, Y512-R515-W660, T514-T520/S524, D534-T648, Y542-Y629/T604, V554-Q558, Q589-E599-K602, I635-N639, D699-R701, N710-A712/S713, T720-C722
π–π interaction	2.65–6.5 Å	F360-Y453-F454, H361-F460, W384-F391-Y512/Y513, F391-F392-F517, F395-Y513, Y401-F405, F403-W507, Y445-W676, W452-Y675, W462-F465-Y469-F470-Y512, F474-Y512, Y512-Y513, F538-Y542-F601, F549-Y629, F603-Y629, H617-F618, W657-W660, Y675-W676, W711-W714
cation–π interaction	<6.0 Å	R683-W702
CH_3/CH–π interaction	2.65-3.01 Å	T267-H312, Q275-F318, H323-L324, F328-V690, W331-V338/P725, P335-W711, Y341-P375, F360-H361, H368-I659, W384-K664, Y405-I439, W452-R456, M402-W507, Q518-W660, Y523-I527, F538-L641, F547-V551, L553-Y590-Q589, F603-G608, W657-K661, W660-K664, M687-W702
Lone pair–π interaction	3-3.7 Å	Y629-T633