

# Supporting Information for

## Temperature-dependent gating pathways in TRPV3

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This Supporting Information includes:

Tables S1, S2, S3, S4 and S5.

**Table S1. Tertiary noncovalent interactions along the PC-dependent gating pathway from K318 to G754 in each subunit of oxidized hTRPV3 with PC bound in the closed state at 4 °C (PDB ID, 8V6K).**

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	E334-R363, E364-K376, E467-K545, K500-E501, E689-R693, D727-R729
H-bond	<3.9 Å donor-H-acceptor <60°	A349/K350-N410-N412, R363-L373, E367-R369, S374-R729, D379-R733, G383-H745, <b>D396-K432</b> , <b>E405-K705</b> , R416-D519, K432-E704, S444-PC-W493, S444-PC-H523, Y448-G558/N561, <b>T456-W559</b> , E466-I469, Q483-R487, Q529-A554, Y564-R567, Q580-Q695, D586-T680, <b>Y594-T636</b> , S620-Y622, D641-L642, N643-Q645/Q646, E679-N683-K686, L707-R712, E719-R733, K722-E725, K743-T744
$\pi$ - $\pi$ interaction	2.65–6.5 Å	Y321-Y359, <b>W433-F441-Y565</b> , F449- <b>F445-Y565</b> , <b>F447-W493</b> , <b>Y448-F526/Y565</b> , F449-F450/W559, <b>Y451-W493</b> , Y460-Y461, R493-PC-K500-PC-H523, <b>W521-F522-Y564</b> , <b>F526-Y564</b> , <b>Y540-Y547</b> , <b>Y564-Y565</b> , <b>Y661-Y594</b> , F597-F601, <b>F601-Y661</b> , <b>Y622-F654</b> , W739-W742
cation- $\pi$ interaction	<6.0 Å	<b>W433-R696</b>
CH <sub>3</sub> /CH- $\pi$ interaction	2.65-3.01 Å	F377-V723, W380-S387, <b>W433-K438</b> , M440-F703, F449-I453, <b>N452-W559</b> , <b>F527-V531</b> , Q570-W692, F590-L673, F597-L664, F625-V629, W692-R696, W710-L711
Lone pair- $\pi$ interaction	3-3.7 Å	<b>H417-E418</b> , W521-PC, F656-T660, <b>T665-Y661</b>

Note: Bold interactions were conserved in closed and open and inactivated states.

**Table S2. Tertiary noncovalent interactions along the PC-dependent gating pathway from K318 to G754 in each subunit of oxidized hTRPV3 with THCN bound in the open state at 4 °C (PDV ID, 8V6L).**

<b>Noncovalent interaction</b>	<b>Cut-off distance</b>	<b>Linked residues</b>
Salt bridge	3.2-4 Å	E364-K366, K376-E736, D379-R733, D391-R729, D396-R716-E704, K500-E702, E631-K634, E689-R693, E709-R712, E736-K738
H-bond	<3.9 Å donor-H-acceptor <60°	E334-R363, Q346-N394, S372-D727, S374-R729, K376-S388, Y390-E736, T399-D400, E405-K705, T411-D512, S444-Y565, Y451-Q529, <b>T456-W559</b> , R464-E467, P470-Y547, T476-Q483, D519-R567, S536-Y547, K545-E546, R567-W692, <b>D586-T680</b> , <b>Y594-T636-Y661</b> , D618-S620, L632-T636/Y661, L707-R712
$\pi$ - $\pi$ interaction	2.65-6.5 Å	Y321-Y359, H426-H430, <b>W433-F441-Y565</b> , F441-F703, <b>F445-Y565</b> , <b>F447-W493</b> -F489, <b>Y448-Y451</b> , <b>Y448-F526</b> , <b>Y448-Y565</b> , F449-F450/W559, <b>Y451-W493</b> /F489, H471- <b>Y540-Y547</b> -H471, <b>W521-F522-Y564</b> , W521-THCN-N561, <b>F526-Y564</b> , F542-Y544, <b>Y564-Y565</b> , F590-Y594, <b>F601-Y661</b> , <b>Y622-F654</b> , W739-W742
cation- $\pi$ interaction	<6.0 Å	W331-R729, <b>H417-R690</b> , <b>W433-R696</b>
CH <sub>3</sub> /CH- $\pi$ interaction	2.65-3.01 Å	K318-Y359, F377-V723, <b>H417-E418</b> , <b>W433-K438</b> , F436-F715, F449-I453, <b>N452-W559</b> , <b>F527-V531</b> , Q570-W692, F590-L673, F597-L664, <b>F625-V629</b> , <b>T665-Y661</b>
Lone pair- $\pi$ interaction	3-3.7 Å	W380-S387

Note: Bold interactions were conserved in closed and open and inactivated states.

**Table S3. Tertiary noncovalent interactions along the PC-dependent gating pathway from K318 to G754 in each subunit of oxidized hTRPV3 with THCN bound in the inactivated at 4 °C (PDV ID, 8V6M).**

<b>Noncovalent interaction</b>	<b>Cut-off distance</b>	<b>Linked residues</b>
Salt bridge	3.2-4 Å	E364-K376, R375-D391-R729, R462-E465, K500-E702, K581-E679, K722-E725, D727-R729, E631-K634
H-bond	<3.9 Å donor-H-acceptor <60°	E334-R363, A348-K353, G352-N415, R363-L373/R375, S374-R729, T378-S747, D396-S402, <b>D396-K432</b> , <b>E405-K705</b> , N410-N412, K432-E704, S444-PC-Y565, Y448-G558, S536-Y547, R567-Q695, <b>Y594-T636-Y661</b> , S621-Q646, D641-L642, E704-R712, S713-R716, K722-A724
$\pi$ - $\pi$ interaction	2.65–6.5 Å	Y321-Y359, <b>W433-F441-Y565</b> , <b>F445-Y565</b> , <b>F447-F489/W493</b> , <b>Y448-F526</b> , <b>Y448-Y565</b> , F450-F489, <b>Y451-W493</b> , Y460-Y461, <b>W521-F522-Y564</b> , W521-THCV-N561, <b>F526-Y564</b> , <b>Y540-Y547</b> , <b>Y564-Y565</b> , Y594-Y661, F597- <b>F601-Y661</b> , <b>Y622-F654</b> , W739-W742
cation- $\pi$ interaction	<6.0 Å	<b>W433-R696</b>
CH <sub>3</sub> /CH- $\pi$ interaction	2.65-3.01 Å	Y321-I356, W331-I373, F377-V723, H417-L694, <b>W433-K438</b> , K435-F715, <b>N452-W559</b> , A520-F524, <b>F527-V531</b> , Q570-W692-R696, F666-L670, P708-W710
Lone pair- $\pi$ interaction	3-3.7 Å	<b>H417-E418</b> , D519-H523, H585-D586, F656-T660, <b>T665-Y661</b>

Note: Bold interactions were conserved in closed and open and inactivated states.

**Table S4. Tertiary noncovalent interactions along the PC-dependent gating pathway from K318 to G754 in each subunit of oxidized hTRPV3 with PC bound in the inactivated state at 4 °C (PDB ID, 8GKA).**

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	E334-R363, D396-K432, K500-E501, E704-R712, D727-R729
H-bond	<3.9 Å donor-H-acceptor <60°	Y321-E334, R337-Q346, A349/K350-N410, G352-N415, R375-T393, K376-Y390, <b>T378-S747</b> , D379-S387/R733, S388-E736, D391-T393, D396-T397/S402, T397-E704, Y409-K705, <b>N410-N412</b> , R416-D519, K432-E704, S444-PC-W493, S444-PC-Y564, T456-W559, S459-R462, D519-R698, W521-PC-Q695, V525-N561, Q529-A554, K545-Y547, Y564-R567, R567-PC-S576, S576-PC-Q695, Q580-Q695, D586-T680, Y594-T636- <b>Y661-Y594</b> , K611-N647, S620-Y622/Q646, S624-S626-D627, E631-K634, K686-R690, <b>E689-R693</b>
$\pi$ - $\pi$ interaction	2.65–6.5 Å	Y321-Y359, W433-F441-Y564/Y565/F703, F445-Y448/Y565, <b>F447-W493-Y451, Y448-F526/Y565</b> , F449-W559, <b>Y460-Y461</b> , W493-PC-K500, K500-PC-Y564, <b>W521-F522-Y564</b> , W521-PC-R567, F522- <b>F526-Y564</b> , F538- <b>F542</b> , <b>Y540-Y547</b> , <b>Y564-Y565</b> , <b>F601-Y661</b> , Y622-F654, W739-W742
cation- $\pi$ interaction	<6.0 Å	F506-R509, <b>R696-W433</b>
CH <sub>3</sub> /CH- $\pi$ interaction	2.65-3.01 Å	F377-K722, A381-H745, T398-F715, Y409-L701, W433-K438, <b>M440-F703</b> , <b>N452-W559</b> , F489-W493, I505-F524, <b>W521-V525</b> , <b>F527-V531</b> , F590-Y594/L673, F597-L664, L605-F654, <b>L632-Y661</b> , W692- <b>R696</b>
Lone pair- $\pi$ interaction	3-3.7 Å	<b>W380-S387</b> , <b>F656-T660</b> , T665-Y661

Note: Bold interactions were conserved in inactivated and pore-dilated states.

**Table S5. Tertiary noncovalent interactions along the PC-dependent gating pathway from K318 to G754 in each subunit of oxidized hTRPV3 with PC bound in the pore-dilated state at 4 °C (PDB ID, 9DIJ).**

<b>Noncovalent interaction</b>	<b>Cut-off distance</b>	<b>Linked residues</b>
Salt bridge	3.2-4 Å	E364-K376, D379-K733, <b>E405-K705</b> , D519-R698, <b>E689-R693</b>
H-bond	<3.9 Å donor-H-acceptor <60°	D322-Y359, S328-N330, N338-L342, T343-Q346, I365-S374, R371-V723, <b>T378-S747</b> , D391-R729, N394-V403, D396-T398, <b>T397-E704</b> , T407-R416, Y409-R698, <b>N410-N412</b> , T411-P510-S511, <b>K432-E704</b> , Y451-Q529, S518-Q695, F522-N561, R567-Q695, M574-S688, <b>Y594-Y661</b> , Y622-K634, E682-K686, E687-R690, G718-C731, K738-T740/H745, E741-K743, D752-G754
$\pi$ - $\pi$ interaction	2.65–6.5 Å	Y321-Y359, <b>W433-F441-Y565</b> , F442-F445, <b>F445-Y565</b> /F569, C446-F450, <b>F447-W493-Y451</b> , Y448-Y451, <b>Y448-F526/Y565</b> , F449-I453, <b>Y460-Y461</b> , <b>W521-F522-Y564</b> , <b>F526-Y564</b> , <b>Y540-Y547</b> , <b>F542-Y544</b> , <b>Y564-Y565</b> , F597- <b>F601-Y661</b> , F594-F633, <b>W739-W742</b>
cation- $\pi$ interaction	<6.0 Å	<b>R696-W433</b> , W692-R693
CH <sub>3</sub> /CH- $\pi$ interaction	2.65-3.01 Å	<b>M440-F703</b> , W493-C496, W521-L584, <b>F527-V531</b> , <b>F590-Y594/L673</b> , F594-L598, <b>L632-Y661</b> ,
Lone pair- $\pi$ interaction	3-3.7 Å	<b>W380-S387</b> , H426-T427, F526-N561, Q645-F654, <b>F656-T660</b>

Note: Bold interactions were conserved in inactivated and pore-dilated states.