Roundtable Name______Pharmacological issues with Connexins/Pannexins___________________

Chairs___Dahl/Spray____

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1

Pharmacological discrimination between connexins, innexins and pannexins:

A) Gap junction blockers were first discovered for invertebrate (innexin) gap junctions, and then observed to also affect connexin made gap junctions and also to inhibit pannexin channels. With the probable exception of heptanol and octanol, all presently known gap junction inhibitors do not discriminate between the three proteins. The number of these inhibitors is limited probably because of unfavorable access of the gap junction structure to extracellular compounds and consequently lack of opportunity for evolution of toxins.
Several agents shown to block connexin gap junction channels have not yet been rigorously evaluated on pannedxins: Arylbenxzoates (FFA, MFA, etc), 2-APB, etc.
B) Because of overlap of action of the drugs on different proteins without sequence homology, they must act on shared domains not recognized by one-dimensional sequence comparison. Question is, do they act at the protein-lipid interface?

2. Point of Discussion 2

Discrimination between connexin "hemichannels" and pannexin channels:

A) At present count there are well over 30 pannexin inhibitors belonging to diverse groups including chloride channel blockers, transport inhibitors, malaria drugs, mitochondrial inhibitors and food dyes. Thus there is a wide reservoir of drugs to differentiate between connexin and pannexin. However, because of the additional effects of most drugs on other targets, identification of a pannexin contribution to a phenomenon on the basis of drug effects may not be unequivocal.
B) "Mimetic" peptides are heavily used to "specifically" interfere with connexins or pannexins. However, connexin mimetic peptides inhibit pannexin channels and pannexin mimetic peptides inhibit connexin channels, such as those formed by Cx46. The number of effective peptides is proliferating and the original idea that the peptides act by docking to the extracellular loops has not been directly demonstrated and has been replaced by even more wacky speculations as to mechanism of actions.. It appears that peptide sequence is less important than the right size, suggesting a rather unspecific steric blocking mechanism.

What were the main conclusions of the roundtable?

Different caveats have to be considered in interpretation of connexin/innexin/pannexin drugs:
a) if possible use multiple diverse drugs
b) even with similar results using this approach another protein may mediate the action of interest
c) drug sensitivity can be modified by accessory proteins (example: pannexin1 and Kv beta subunit)

Was an email group set up? ***YES*** **X** ***NO***
If yes, whose email should be used for contact?_________________________________

Roundtable Name: ______Structure/Function Relationships and Issues__________

Chairs: _____Yeager, Harris____

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1

Explanations for the different predictions of the major pore-lining helix from different types of accessibility studies

2. Point of Discussion 2

Possible differences in the structure, gating properties and modulatory sensitivities between hemichannels and junctional channels.

What were the main conclusions of the roundtable?

Connexin channels are difficult to study.

The channel is not modular and one should not expect that modifications at one location in the channel will not affect processes that involve other parts of the channel.

Was an email group set up? ***YES*** **X*****NO***

Roundtable Name___Translational Research_________________

Chairs: Robert Gourdie (VTCRI, VA) and Gautam Ghatnekar (FirstString Research, SC)___

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1:

General discussion of translational research
What is translational research ?
What are the barriers to translational research ?
Commercial vs non-commercial translational research ?
Clinical vs commercial translational research ?
What and why patent discoveries ?
What are the steps to filing a patent and commercializing a discovery ?
How to go after funding for translational projects

2. Point of Discussion 2:
Translational Research in Relation to Connexins and Pannexins
What are the new emerging areas of translational research in connexins and pannexins ?
Clinical trials on connexin targeting drugs in myocardial infarction – Zealand.
Clinical trials on connexin targeting drugs in skin wound healing –CoDa, FirstString.
Pre-clinical studies in eye, heart, macular degeneration and spinal chord look promising.
Identification of disease-causing mutations in connexin and pannexins in humans.
Encouraged trainees in turn to contribute a POV to the discussion.

What were the main conclusions of the roundtable?
The discussion was wide ranging, interesting and no hard conclusions were reached. There was some discussion of over what translational research is –it apparently has different meanings for different individuals. Some placed more emphasis on clinical translation others saw the role of commercialization as central. View point tended to depend on the speaker

There was agreement over the difficulty of translating a basic research finding. How do you find the right people to assist you with writing patents, commercializing a discovery etc.

Some around the table described the necessity for patenting in order encourage translation of discovery. Without protection of IP, no investment will occur.

Was an email group set up? ***YES*** **X*NO***
If yes, whose email should be used for contact?______________________________________

Roundtable Name: Wound Healing

Chairs: Green and Laird

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1:

Wound healing was discussed mainly in the context of the skin with references to diabetes and occasional reference to cancer and cardiovascular.

Discussion focused around the use of antisense to transiently down regulate Cx43 in wound repair. Transient and not chronic down regulation of Cx43 was deemed to be key to accelerated wound repair but it appeared that no other connexin family members have been studied in any detail with the exception that antisense to Cx31.1 has been reported to increase skin thickness. The question was raised as to whether other connexins (besides Cx43) in the skin might be good therapeutic targets and what about pannexins?

2. Point of Discussion 2:

Considerable discussion was placed on the use of mimetic peptides to connexins as a means of therapeutic intervention. Worries were expressed that high concentrations of the peptides could, and maybe do, have off target effects but many studies get good connexin down regulation at low peptide concentrations. Gap26 was discussed as a more pan mimetic peptide for connexins while some suggested that Gap27 was more specific and both were effective at 5-10 μM.
Some questions and comments raised:

- Do mimetic peptides have broader effects than appreciated?
- Is the effect of mimetic peptides based more on hemichannel knockdown rather than gap junction channel knockdown?
- Could pannexins be a first response channel followed by connexins? Thus, should we consider pannexins as a therapeutic target?
- The slower turnover of pannexins compared to connexins may be important in therapeutic designs.
- The field still suffers from good therapeutic, non-toxic up-regulators of connexins and pannexins.
- Specific distinguishing pharmacological blockers of connexins and pannexins remain an issue of considerable concern.
- Why do Cx43 levels appear to decrease in aging skin?

What were the main conclusions of the roundtable?

The group recognized that therapeutic intervention where connexins (and maybe pannexins in the future) is important, and the skin and cornea are great target tissues to study wound repair given their accessibility to the use of creams, gels and solutions.

As a field, it was deemed very important to foster connexin/pannexin therapeutics as this will help drive the field as a whole and stimulate a broader interest in these large-pore channels.

Was an email group set up? ***YES*** **X** ***NO***
If yes, whose email should be used for contact?

Roundtable Name___CORRECT AND FUNCTIONAL PROTEIN INTERACTION________________

Chairs_________ISAKSON AND SHAW____

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion:

--pannexin appears to have much different properties than connexin in terms of protein interactions
→evidence appears to indicate in many systems that pannexins can amplifying receptors after activation

--connexin ER different than connexin in Golgi different than connexin in membrane, and the protein-protein associations at each spot is different—so the detergents used for e.g., co-immunoprecipitation need to be specifically determined for correct connexin binding partners

--co-immunoprecipitation is basically incremental, one alternative is blue native page analysis another is size exclusion

--put another way, there is a huge DIFFERENCE BETWEEN FINDING BINDING PARTNERS AND DEMONSTRATING FUNCTIONAL BINDING PARTNERS

--can you do comparative connexin isoform work? i.e., can one connexin be compared to another? Probably not, eg. Cx43 and ZO-1 are probably completely unique to Cx43 and not other isoforms.

What were the main conclusions of the roundtable?

--there is a real need to drop bias and focus on function, function, function—focus on BOTH transgenic connexin mice AND established mouse disease models AND human disease states

Was an email group set up? YES NO

***If yes, whose email should be used for contact?*______________________________________**

Roundtable Name___Emerging roles for pannexin/connexin metabolism _________________

Chairs_________Martin, Leitinger ____

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1:

Discussion focused largely on ATP release and signaling events via Panx and Cx channels with impact on diverse tissue networks.
Ross Johnson reminded us of previous details on metabolic labeling of cells relating to cell growth characteristics
Discussed potential of other signaling molecules that may emerge to be critical in metabolic processes that may also be transmitted

Highlighted how different tissues respond differently—could be important for interpretation of results

2. Point of Discussion 2:

Major focus of discussion was a need for consensus on measurement of ATP in cells and tissue – and concentrations seen in in vitro expts.

What were the main conclusions of the roundtable?

No major conclusions were made – recognition that this is a novel and important emerging area - is it better to inhibit of activate channel activity was a key question and as tools emerge capable of doing both careful choice, understanding of tissue system and network targeting needed.

Was an email group set up? YES x NO - but it could be
If yes, whose email should be used for contact?___patricia.martin@gcu.ac.uk

IGJC Meeting July 13-18th

Monday July 15th – Round Table 7 – Connexin Phosphorylation

Session Chairs:

- Paul D Lampe –plampe@fhcrc.org (P. Lampe Lab).
- Scott R Johnstone – Scott.johnstone@glasgow.ac.uk (S. Johnstone Lab)

Registered Attendees:

- Elizabeth Mitchell ehm08@uab.edu (R Serra Lab)
- Miranda Good – mgood@email.arizona.edu (J. Burt Lab)
- Paul Sorgen – psorgen@unmc.edu (P. Sorgen Lab)
- Hanjun Li – hanjun.li@unmc.edu (P. Sorgen Lab)
- Parul Katoch – pkatoch@unmc.edu (P Mehta Lab)
- Anuttoma Ray – anuttoma.ray@unmc.edu (P Mehta Lab)
- Parmender P Mehta – pmehta@unmc.edu (P Mehta Lab)
- Morten Schak Nielsen – schak@sund.ku.dk (M. Nielsen Lab)
- Richard Benninger – richard.benninger@ucdenver.edu (R. Benninger Lab)
- Mona Al-mugotir – mona.almugoitr@unmc.edu (P. Sorgen Lab)
- Rengasayee Veeraraghavan – saiv@vt.edu (R. Gourdie Lab)
- Michael Bennett – Michael.bennett@einstein.yu.edu (M. Bennett Lab)
- Anastasia Thevenin – ant212@lehigh.edu (M. Falk lab)

Discussion 1: Cx32 and phosphorylation.

- Cx32 Tyr 243 site is dephosphorylated by tyrosine phosphatase.
- Cx32 stable transfected (pCDNA) into Hela cells.
  - pCDNA is not always the best for stable transfections.
- Using phospho-mimetic glutamate (not aspartate).
  - Discussed that glutamate is a better analogue.
  - Produces channels opening, not closing.
  - Concerns that it is only in one cell line, is this enough to prove pore opening.
- PKA mediate phosphorylation regulates GJ opening, following forskolin treatments.
- AMPK mutants, is it causing a change in the half life of the proteins.
  - Which 2 sites are required?
- Where in the cell is it happening.
  - Require a phospho-specific antibody to prove.

Discussion 2: Cx36 and phosphorylation.

- Discussion raised by Mike Bennett.
- Which antibodies are available?
  - John O'Brien has a couple of phospho-specific antibodies.
- One Ser-Ala mutant produces no effect.
  - Asp and Glut, not always effective.
  - Should also try Ala mutations.
- Change in phospho status, is not sufficient/ necessary for Mg^{2+} efficiency.
- Res- sites early in the C-term.

Discussion 3 – Cx43 S262 as a MAPK site.

- Discussion raised by Scott Johnstone.
- Paul Lampe states that mouse S262 is probably a MAPK family site.

  - Experiments demonstrating PKC activity use PMA, which induces a signaling cascade – assumed that PKC specificity at this site is not specific.
- Anastasia Thevenin noted that in Humans the S262 is may not be a MAPK site as it is not followed by a Proline, which is usual for MAPK binding/ activity.
  - Therefore there are 4 MAPK sites in mice and rats and maybe only 3 in human.
  - Is there any experimental data to demonstrate this?
  - Follow up note by Scott Johnstone: Some studies demonstrate proline is not necessarily the only controlling point in MAPK activity. Studies showing proline to alanine in some proteins on cause minor alterations in MAPK phosphorylation. Therefore it is not clear but suggested that this proline to glutamine substitution in humans means that S262 is not a MAPK target. Experimental data would be required to show this.

Discussion 4: Cx43 phospho-specific antibodies.
- Discussion raised by Paul Lampe.
- Best phospho antibodies:
  - Lampe lab has a number of phospho-specific antibodies.
  - Seems the Santa Cruz 255 and 262 detect phosphorylated Cx43 in western blots and labeles junctions in IF but also nuclei in some cells.
  - Santa Cruz 279/282 very poor sensitivity.
  - Santa Cruz Tyr antibodies are poor.
  - S368 antibodies are available from many companies and many work well.
  - The existing Cell Signaling S368 antibody has seen some recent reductions in quality and may be associated to poor/ late bleeds.

Discussion 5: Requirement for making phospho antibodies.
- Do you need specific residues around the sites to make a phospho-antibodies.
  - Paul Lampe answered that typically you use a phospho-mimetic at the site followed by 3 residues surrounding the site.

Discussion 6: Could structural changes affect antibody binding.
- Discussion raised by Linda Matsuuchi.
- Linda has observed that in some conditions the antibody may not work.
- Could there be a masking effect of protein folding on the antibody?
- Could nearby serine phosphorylation cause failure of antibody to work?
  - Paul Lampe stated that this may be the case – wouldn't be surprised.

Discussion 7: Does phosphorylation lead to instability of the protein in the heart and other cells.
- There are distinct populations of phospho-Cx43.
- There is not a one for all solution, but it is thought that loss of certain phosphorylation sites in the heart leads to increased internalization (opposite to what has been reported in others) or that some are pro-internalization.
- How do we resolve if Cx43 Phosphorylation is doing different things at different sites e.g. can the same site function for insertion or removal from the membrane?
    - Klaus Willecke did Aspartate and Alanine events.
- Differences can be seen in Cardiomyocytes and cardiac fibroblasts e.g. cell specific effects.

Discussion 8: Does phosphorylation play a role in slower than expected band migration on Western Blot?

- Discussion raised by Scott Johnstone.
- Observed that in smooth muscle cells the MAPK sites / antibodies detect a single band closer to 50kDA than expected for P1/P2 bands (commonly associated Cx43-phospho bands by Western).
    - Paul Lampe states that shifts of up to 8Ka can be seen with phopsohrylation particularly during mitosis.
- S368 does not cause shifts by WB (e.g. can be seen in the P0 and other bands).
- Shifts are seen when Cx43 phospho-mimetics are made.
- Typically it was shown that greater than 2 sites are required to create a shift in banding pattern by Western blot.
- Multiple site phosphorylation together or phosphorylation with prolines can cause it to run at different heights by Western.

Roundtable Name___Session 2:RT3: Pannexin/Connexin electrophysiology_________

Chairs___Rich Veenstra and Doug Bayliss__________________________________

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1

How do pannexin1 channels open physiologically –distinction made between basal and voltage activated channels,
high positive voltages > +20-30 mV are not physiological,
caspase cleavage may be related to apoptotic events and is non-reversible,
basal activity is reversible,
panx1 channels open in physiological calcium (unlike WT connexin channels)
what is the conductance of panx1 channels?
Multiple conductances observed, from 50 to 110 pS, may reflect number of subunits gated open
Do pannexins form gap junctions? Glycosylation sites probably the limiting factor in vivo

2. Point of Discussion 2

What is the best blocker of panx1 channels? Blue dye IC 50 is 0.3 micromolar
Gap27 was best connexin HC blocker until one of today's talks
Use D/N constructs to knockdown function of panx1/cxn channel in question to help distinguish between channel types
What are the best cell types to study these single membrane channels?
HEK293 cells express plenty of Cx43, N2a cells have endogenous panx1
Rin cells may be the most connexin- and pannexin-deficient cell line

What were the main conclusions of the roundtable?

Useful and informative discussion, lively, numerous contributors

Was an email group set up?   YES   X NO

If yes, whose email should be used for contact?_______________________________________

Participants included Alex Lohman, Nick Weilinger, Roger Thompson, Donglin Bai, Gerhard Dahl, Jose Ek Vitorin, Mike Bennett, Felix Bukauskas, Eliana Seemes, Amal Bera, Kodi Ravichandran, Yu-Hsin Chiu, Masakatsu Watenabe and perhaps a few unnamed participants

Roundtable Name: Physiological roles for heterotypic/heteromeric channels

Chairs__________Burt & Koval____

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1: Are there convincing *in vivo* examples of heteromeric or heterotypic channel formation?

Cx40 and Cx43 in the atria, Cx40 and Cx37 in endothelium were discussed based on co-localization of these proteins, but convincing evidence for formation or function of heteromers or heterotypic junctions *in vivo* is not available. Available data support functionality of Cx40/Cx43 heteromeric channels but functional features that would allow their distinction in *in vivo* setting have not been identified.

Heteromeric Cx32 and Cx26 connexons have been isolated from the liver. *In vitro* studies of these channels suggest functional differences but data are limited and again distinguishing features that would allow assessment of their importance *in vivo* are not available. Biochemical evidence of Cx46/Cx50 heteromers from lens was also mentioned, although it is unclear whether the majority of the channels in native lens are heteromers or homomers based on this criterion.

Can their function be distinguished from homomeric/homotypic channels *in situ?*

Need new clever approaches or more knowledge from *in vitro* systems on functional differences that can be implemented *in vivo*. The gold standard would be measuring endogenous substrates diffusing through the channels, but this is difficult to do directly. There is a need for novel reporter assays. Utility of concatenated connexins as a tool to measure permeability of channels with defined stoichiometry was discussed and contrasted to concatenated pannexins, which were shown at the conference to work well. One concern is that the conformation of the N terminus of connexins tucked into the pore of the channel may make the concatamer approach difficult.

2. Point of Discussion 2: Are there cell- and connexin-specific differences in the assembly of gap junction channels? Do differences in site of assembly demonstrated for two connexins in a specific cell type apply to other cell types?

Again, there are limited data to suggest that chaperones operative in one cell type are necessary or sufficient in other cell types. Differential handling of beta connexins vs. alpha connexins suggests at least two distinct quality control pathways, however it is likely that heteromer formation is regulated by differential interactions of compatible connexins with the same quality control pathway.

What were the main conclusions of the roundtable?

There are convincing data from *in vitro* studies that heteromeric connexons and heterotypic junctions can form; it remains unclear whether they form in all settings where connexins are co-expressed. It also remains unclear what advantages are conferred if they do form. In part this reflects uncertainty on gating and regulation of channels – fundamental questions on structure-function of any given connexin limit interpretation of heteromeric/heterotypic channel data (which domain(s) comprise which gates for the channel; where the CT comprises the gating particle, which domains comprise the receptor for the gating particle; how many CT particles comprise the gating particle, 1, 2, 6?). A more straightforward mechanistic role for heteromer formation is the potential for regulating cell network formation (intercellular connectivity) by altering heterotypic compatibility.

Was an email group set up? ***YES*** **X*NO***

If yes, whose email should be used for contact?____

Roundtable Name Non--junctional/non-channel Connexin function

Chairs__Jean Jiang and Mario Delmar_________________

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1

describe here

A. Disease-related mutants of connexins

Observations:

A. Some without channel functions exhibit similar properties and roles as the other mutants which have full or partial channel functions.

B. Non-channel forming, connexin C-terminus by itself has certain functions, including inhibition of cell proliferation and differentiation, etc in tumorigenicity, heart and lens.

2. Point of Discussion 2

describe here

A. Role of connexins in mitochondria.

The points we discussed including: What is the functional importance, how it is transferred to the mitochondria, what is the membrane topology of the connexin in this organelle and if it forms channels?

B. Role of connexins in nucleus.

We did not discuss further on this topic.

What were the main conclusions of the roundtable?

1. In addition to forming channels, connexin with short half-life could function as a regulatory protein and non-channel forming part of the connexin could be just as important as channel-forming parts.

2. More evidences of channel-independent function of connexins are emerging. To prove or disprove, we have to provide more, better controlled data and also be open-minded.

Was an email group set up? YES X NO

If yes, whose email should be used for contact?____

Roundtable Name________Pannexin posttranslational modifications_________

Chairs_____Silvia Penuela and Roger Thompson______________

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1

The main point of discussion was the role of glycosylation in limiting pannexin's ability to form gap junctions and also effecting trafficking. While the panel all agree that glycosylation is important in regulating trafficking, the point was raised that it is still unclear if unglycosylated forms make it to the cell surface. And if they do, are they able to form patent junctions. Currently gap junction analysis is limited to expression systems and identifying panx junctions in tissue or in vivo will be critical for answering this question.

2. Point of Discussion 2

The second point(s) of discussion centred around understanding the role of more traditional posttranslational modifications in pannexin function. These included phosphorylation, nitrosylation and others (ubiquitination / palmitoylation). To date the strongest evidence exists for nitrosylation, but it is still not clear if this involves nitrosylcystein or nitrosyltyrosine (or both). There is strong evidence that kinases regulate pannexin function, but direct evidence for phosphor-pannexin is still lacking. Difficulties with immunoprecipitation from tissue (i.e brain) were raised and the panel agreed that this is the limiting factor for these levels of analysis. The possibility of direct allosteric modifications of pannexin by kinase binding (or other proteins) and c-terminal cleavage was raised. There was some concern that Ravichandran's work has not been reproduced by others – however it is important to note that cleavage may be a specific modification under select circumstances.

What were the main conclusions of the roundtable?

More work is required to fully understand the impact of posttranslational modifications. In particular, the chairs suggested that the greatest impact will be learned when in vivo or tissue assays are optimized.

Was an email group set up? ***YES*** X ***NO***

If yes, whose email should be used for contact?__agreed to use the meeting's list of emails for further contact between attendees if desired. ___________________________________

Roundtable Name___Connexin Hemichannels Regulation________________

Chairs_________Luc Leybaert and Juan C. Sáez

What are the two primary points of discussion/debate that occurred?

1. **Point of Discussion 1: What is missing to see connexin hemichannels functioning under physiological conditions?**

First, it was proposed to identify a criterion to identify connexin from pannexin hemichannels. Then, it was discussed that regulation of connexin hemichannels might require specific molecular machinery co-express with connexins, which might be absent in exogenous expression systems such as xenopus oocytes and connexin deficient mammalian cell lines. One example is that glucose rapidly increases the activity of Cx43 hemichannels in tanicytes but not in cortical astrocytes or Cx43 HeLa cells tranfectants. For demonstrating the involvement of Cx hemichannels it is necessary to use different approaches, including classical inhibitors, peptides homologous to extracellular and intracellular domains of Cxs, conductance measurements, siRNA and/or cells of Cx K.O. animals, , antibodies, etc… the more the better. The present need of specific blockers was mentioned. Related to this, we discussed the fact that connexin hemichannel opening is likely to be a concerted action with activation of other channels (f.e. Panx1 channels) or release mechanisms at the same time. Therefore, inhibition of f.e. ATP release by Cx hemichannel-inhibiting approaches does not necessarily mean only hemichannels are involved in this particular response. The same applies for Panx channels. The fact that Cx hemichannels as well as Panx channels are calcium ion permeable channels makes it very likely that (hemi)channel opening activates other membrane transporters and release mechanisms. This should be be further considered in order to get a finer grained picture of the contribution of these channels to physiology as well as pathology.

2. **Point of Discussion 2:**

Relationship between conductance and permeability: Although there is some correlation in many cases this correlation is poor and we need to characterize permeability properties of hemichannels with a resolution similar to that of unitary conductance measurements. A possible way would be using expression of connexins conjugated to specific reporters including Ca^{2+}, redox etc…, which are available, and the used of high resolution microscopy to monitor changes at the channel level.

What were the main conclusions of the roundtable?

Was an email group set up? YES ■NO

If yes, whose email should be used for contact?____

Roundtable Name Table 2-6 Internalization/degradation pathways of connexins/gap junctions___

Chairs______Falk / Berthoud___

What are the two primary points of discussion/debate that occurred?

1. Point of Discussion 1

describe here
We discussed:

- to use correct nomenclature when addressing proteins (connexins), hemi-channels, and gap junction plaques. This is important because different internalization and degradation pathways may be used for these structures
- we discussed internalization mechanisms (clathrin-mediated) and non-clathrin mediated (lipid raft based) or unknown and which pathway is likely to internalize what structure

- we discussed cellular degradation pathways (proteasomal, endo-/lysosomal, and autophagosomal. What each pathway is designed for, and what structures are likely to be degraded by each one

2. Point of Discussion 2

describe here

We mostly clarified how these pathways work, what cells use them for and what Cx, connexon, and GJs are likely to use for internalization/degradation.

What were the main conclusions of the roundtable?

The different pathways were reviewed, likely pathways defined, and participants were urged to keep an open mind. Also, participants were urged to do necessary controls, especially if evidence for an unusual or novel pathway is obtained.

-Especially students were very thankful for the discussions and clarifications! Overall, the table and discussion was a hit! Definitively repeat in 2015!

Was an email group set up? YES **X** ***NO***

If yes, whose email should be used for contact?___________________________________