Tumor cells become oxidative pentose cycle, therefore cytoplasmic free water dependent, when their defective mitochondria disrupts low deuterium metabolic water use from the matrix and they switch to consuming pentose cycle-derived NADPH for reductive DNA and nuclear membrane fatty acid synthesis. Metabolic water by complete fat oxidation, coupled with complex-IV, contains low average ~115 ppm (parts per million) deuterium due to deuterium discrimination during photosynthesis in food. We herein report that monodeuterated, 100 ppm, 50 ppm and 25 ppm extracellular (free) water treatment significantly decrease nucleotide and nuclear membrane sterol and lignoceric acid effects in comparison with natural 150 ppm deuterium containing water via the oxidative branch of the pentose cycle. This recapitulates metabolism after genetically restored mitochondrial luminar hydratase in clear cell kidney tumors and mimic the metabolic impact of Gleevec (imatinib mesylate, STI-571, Gleevec) and metformin treatments in other tumors.

**Model & Methods**

Cytoxic effects of DDW containing D at a concentration of 25 parts per million (ppm), 50 ppm, 105 ppm and the control (150 ppm) in MIA-PaCa-2 pancreatic cancer cells were monitored by the real-time cell impedance detection xCELLigence method. Nuclear membrane turnover and nucleic acid syntheses were determined by targeted [1,2-14C]-D-glucose fucose analogs and compared with Gleevec, restored fumarate hydratase and Metformin effects, respectively, in the metabolic network as shown below.1-3

**Patients with inoperable PaCa**

The median age of the 32 DDW treated patients was 61.5 years. Median duration of the treatment with DDW was 6.64 months (86 ppm, 65 ppm and 45 ppm regimen DDW). The treatment period showed a high standard deviation (SD: 12.24 months), because 9 patients (28%) consumed DDW for an extended period, more than one year. Patients started the DDW treatment at different time points at their free consent after diagnosis, which was recorded. The median elapsed time between diagnosis and entering the trial was 1.16 months (SD: 4.06 months). When data sheets were closed for standard matrix diagnostics, data processing and abstracting, in order to meet study deadline objectives (June 2011), 17 patients were still alive and offered continued DDW treatment; therefore they are included in this report with their applicable (at least) mean survival time upon study termination.

The median age of the 30 control natural deuterium-containing water consuming patients was 65.9 years (SD=9.05 years) (Female: n=16, Average age: 67 years, SD=8.24 years; Male: n=14, Average age: 64.3 years, SD=8.9). Histology in all cases confirmed pancreatic adenocarcinoma and all patients received treatment with standard gemcitabine (Gemzar 1000 mg/m2 as an intravenous infusion) combined with 5 fluorouracil consistent with the EU gastrointestinal adenocarcinoma disease management protocol.

**Results**

All extra-mitochondrial NADPH synthesis pathways are targeted by DDW; particularly that of the direct glucose oxidation pathways, the pentose phosphate pathways, cytoplasmic fumarate hydratase and the serine oxidation glycone cleavage reactions to repair oncogenic NADPH producing glycolysis. Deuterium depleted sugars and water may be included as non-toxic anti-cancer treatment modalities for prevention and treatment.